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VOL. 34, NO 1 March, 1959

THE QUARTERLY REVIEW *of* BIOLOGY

GADOW'S ARCUALIA AND THE DEVELOPMENT OF TETRAPOD VERTEBRAE

BY ERNEST E. WILLIAMS

Museum of Comparative Zoology, Harvard University

ABSTRACT

Critical reexamination of Gadow's theory of the composition of vertebrae from four pairs of arcualia is inapplicable to tetrapods and so remote from the facts that his terminology even in modified form should not be employed in tetrapods. Division of the sclerotome into anterior and posterior parts by a sclerocoel is probably primitive in tetrapods. The origin of adult vertebral structures from these sclerotome parts is always complex. Centra in tetrapods are not arch centra, but autonomous structures, primitively two per neural arch, a hypocentrum formed from perichordal tissue belonging to the cranial and caudal halves of a single sclerotome, and a pleurocentrum formed from perichordal tissue from the caudal half of one sclerotome united with perichordal tissue from the cranial half of the next succeeding sclerotome. The main body of the neural arch of tetrapods is either wholly derived from the paraneural tissue of the caudal half of a single sclerotome or from this plus paraneural tissue from the cranial half of the next succeeding sclerotome. The pre- and post-zygapophysial articulations form within the cranial halves of sclerotomes. Ventral arches, when present, are formed either from tissue from both halves of a single sclerotome or from one or the other half. The neural arch is homologous throughout the tetrapoda, living and fossil. The functional centrum, if there is a departure from the primitive condition with two functional centra, may be either the hypocentrum or the pleurocentrum. The evidence suggests that the hypocentrum became the functional centrum only in one branch of the tetrapoda which died out at the end of the Triassic and that all living tetrapods—the three orders of Amphibia and the Amniota—retain the pleurocentrum as the functional element. It is therefore suggested that the living Amphibia, on the basis of vertebral structure, are more closely akin to the Amniota than to the Paleozoic Amphibia termed Rhachitomi and Stereospondyli.

IN 1895 Gadow and Abbott proposed a theory of the morphology of vertebrae which in their estimation was valid for the whole series of vertebrates. In 1896 Gadow explicitly applied this theory to tetrapods. In the more than 60 years since the appearance of these two papers our knowledge of the actual process of development of tetrapod vertebrae has been greatly clarified and extended, so that the basic facts are on record and the areas of dispute have been narrowed. Yet it is still impossible to find in the literature any summary that gathers together the evidence for all the tetrapods and that, facing the problem of the interpretation of this evidence, squarely pits fact against theory. In consequence a most remarkable confusion exists in the secondary literature, particularly in textbooks, so that the outdated

concepts of Gadow are accepted as fully valid or are combined in an incomplete and unsatisfactory fashion with more modern embryological concepts. In the original literature individual studies of great merit are often overburdened with theory that may be applicable only to the specific class or even animal studied. More than this, there is at present a thoroughly unnecessary contradiction between embryological and paleontological theories of vertebral morphology and history.

I attempt here a summary of the embryological evidence for tetrapods. It is true that summaries already exist, and that some of them (Goodrich, 1933; Remane, 1936; Devillers, 1954) are quite good.

Goodrich's is the best account in English. Devillers', though much compressed, is excellent, but Remane's will probably long remain the best account in any language. Quite apart from valuable and perceptive discussion it is by far the best reference work on the total field.

They are good, however, within the framework of a special limitation—that none of the summarists has been able to free himself entirely from the incubus of Gadovian theory. It is necessary to make clear, once and for all, that Gadow's hypotheses as applied to tetrapods are very remote from the facts, so remote that even a superficial adherence to his terminology complicates with false simplicities a story that, sadly enough, cannot, given the modern evidence, ever again have the tidiness seemingly given it by Gadow's four pairs of arcualia.

Gadow's theory of the composition of vertebrae has, in fact, the same fatal and fallacious beauty as the vertebral theory of the skull, demolished by Huxley on embryological evidence somewhat less than one hundred years ago. A similarly destructive task is necessary here, and the same kind of evidence must be employed. Once we know with perfect clarity what vertebrae are not, we may begin again with the abundant evidence already available to discover what vertebrae are and what their history has been. The new synthesis, however, is itself a secondary and not a primary task and will not be attempted here and now. Rebuilding can be attempted only after the ground is cleared.

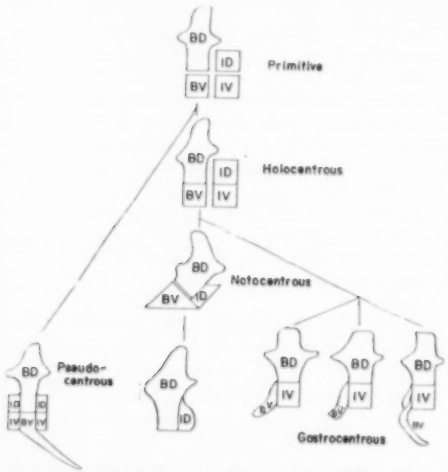

FIG. 1. GADOW'S SCHEME OF VERTEBRAL EVOLUTION
BD, basidorsal; BV, basiventral; ID, interdorsal; IV, interventral.

THE CLASSIC THEORIES

I cannot here present a history of the theories of tetrapod vertebral morphology, since such a history could hardly be more than an annotated chronological list of the individual original workers in a field in which each investigator has had his own somewhat individual theory. Perhaps the clearest understanding of the present state of this phase of comparative anatomical theory will be obtained by a statement of the views (and the defects of those views) of the three most influential workers in the field: Gadow, Schauinsland, and Piiper.

1. The first of these, perhaps the most pervasively influential, has been Hans Gadow.

I omit discussion of the posthumous book by Gadow (1933). It was intended as his own attempt to reconcile his early views with those of Piiper and his school; as regards fundamental points, it is more nearly a surrender than a reconciliation and as such does not need special attention. A handsome, rambling, fascinating compendium of miscellaneous observations, mainly on adult vertebrae, spiced with theory and argument, and in part self-contradictory, the book was never finished by its author and is not justly chargeable to him.

Gadow (1896, p. 50) stated very succinctly his basic theory (Fig. 1):

The key to the solution of the composition of the vertebral column is given by the metameric repetition of the four pairs of symmetrically ar-

ranged cartilaginous elements the origin of which we have traced in Fishes, namely:

One pair of basidorsalia.

One pair of basiventralia (with its lateral outgrowths = ribs or pleurapophyses and haemal ventral outgrowths = haemal arches, chevrons, wedge-bones, haemapophyses).

One pair of interdorsalia.

One pair of interventralia.

The first of these four pairs is always present and forms the neural arch. Of the other three pairs any one may be suppressed, sometimes even two in the same skleromere.

Thus Gadow's primary assumption was that the basic pattern of tetrapod vertebral structure had already been given in fishes—*specifically in elasmobranchs and ganoids*—and that all further evolution in land vertebrates was by reduction or loss of elements of this basic structure.

In tetrapods Gadow distinguished four types of vertebrae:

I. All four pairs of arcualia are present as separate pieces, of which the interventralia are smallest e.g. tail of *Archegosaurus, Sphenosaurus, Chelydosaurus.*

II. The interventralia are suppressed.

A. The other three pieces remain separate and the interdorsalia tend to form the centrum (Notocentrous type) e.g. trunk of *Euchirosaurus, Archegosaurus, Actinodon, Trimerorhachis.*

B. The three pairs of basidorsalia, interdorsalia and basiventralia co-ossify, e.g. trunk of Anura.

C. The interventralia and basiventralia are suppressed. Such "epichordal" vertebrae consist of dorsal elements only, e.g. trunk of *Pipa, Xenopus, Bombinator.*

III. All the four pairs of arcualia are present but the interbasalia [interdorsalia + interventralia] form neutral zones of intervertebral cartilage (Pseudocentrous type), while—

A. The basidorsalia and basiventralia fuse together and form the middle of the vertebral body, e.g. tail of Urodela.

B. The basiventralia are suppressed, e.g. trunk of Urodela.

IV. The interdorsalia are reduced. The interventralia are enlarged and form the centrum. (Gastrocentrous type.)

A. The three remaining components ossify separately and remain separate; the basiventralia are still large and carry most of the neural arch. (All the vertebrae of *Eryops, Cricotus,* the atlas of the Amniota.)

B. The centrum is much enlarged, forms the whole of the "body" and carries the neural arch (neurocentral suture). The basiventralia are much reduced and form the "intervertebral disks" or menisci, attached to the cranial edge of the centrum; when less reduced, they appear as the so-called wedge-bones, "intercentra," or chevrons. (Trunk and tail of most Amniota.)

C. The centrum and neural arches alone constitute the vertebra, the basiventrals are lost completely. (Trunk of many Amniota, for instance, the thoracic and lumbar vertebrae of lizards, caudals of many mammals and birds.)

When Gadow's 1896 paper, of which these are the conclusions, is critically examined, certain radical deficiencies appear.

Particularly serious is his nearly complete ignorance of the embryology of the vertebral column in the Amniota. He was indeed able to present short summaries, based on nearly adequate material, of vertebral development in the Anura and Urodela, but for the Amniota his few sectioned embryos were late stages of lizards and were intended rather to demonstrate the microanatomy of the vertebrae in these forms than to illustrate the ontogeny of their vertebrae. For vertebral development in birds he limited himself to a digest of a paper by Froriep (1883), while for mammals he had only the papers of Froriep (1886) and Macalister (1893), the latter concerned with the atlas-axis problem. He failed even to cite in his bibliography most of the important embryological studies which preceded his own work. He had, indeed, in his earlier paper (Gadow and Abbott, 1895, p. 187) commented with brusque grandiloquence on two of the students of the embryology of vertebrae in Amniotes, namely, von Ebner and Corning. He dismissed von Ebner's discovery of a transverse split in the sclerotome with sweeping (and erroneous) rhetoric:

> I have no hesitation in stating categorically that nobody has even seen a transverse splitting within a sklerotome, dividing the latter into 2 successive halves, and that nobody has ever observed a healing up or recombination of these halves. The assumption of such a split and fusion offered itself as a theoretical necessity, simply in order to explain the actually observed overlap of myomeres and skleromeres. That which was crudely observed to take place in the axial cartilage of comparatively late stages of Sauropsida was, so to say, projected by mental reflection upon the progenitors of this cartilage, namely upon the sklerotomes.

2. The year 1905 produced the second very influential work on vertebral morphology. In that year H. Schauinsland, in a review article in Hertwig's *Handbuch*, summarized the extensive embryological literature so woefully neglected by Gadow. He accomplished a real and very notable synthesis of previous contributions, but his work went beyond this. He had himself published on the development of the skeleton in *Sphenodon*, and for the review article he undertook at least a certain amount of original work in each vertebrate class. Most of the many excellent illustrations in his paper were new.

Schauinsland was aware of Gadow's work but was unappreciative. He only infrequently refers to Gadow (1896) or to Gadow and Abbott (1895), and he does not use Gadow's terminology, but mentions it only in the synonymy of other less formal terms.

Apparently Schauinsland was led to this negative attitude toward the findings of Gadow and Abbott by their strange conception—later surrendered by Gadow himself (1933)—that the sclerotome in all vertebrates arose from an S-shaped stage of the somite. In regard to this suggestion Schauinsland (1906, p. 422) commented: "Es thut vor allem Not, dass die Gadowschen Angaben in seinen sonst vortrefflichen Arbeiten, bevor sie zu einer Grundlage für die Betrachtung der Wirbelsäulen-Genese gemacht werden können, durch gute, die Präparate wirklich wiedergebende Abbildungen, anstatt durch rein theoretisch konstruirte diagrammatische Skizzen oder Wirbelanalysen erläutert werden, deren Verständnis überaus schwierig bleibt." (Compare Gadow's comment on von Ebner, above.)

Schauinsland nowhere epitomized his own findings with the neat clarity of Gadow. However, like Gadow, Schauinsland was sure that a single pattern underlies vertebral structure in all vertebrates. He stated at the beginning of his review paper: "Vergleicht man das Achsenskelett eines Cyclostomen etwa mit dem eines Säugers, so erscheint es auf ersten Blick fast unmöglich, das eine auf das andere zurückzuführen und dennoch sind sie durch Uebergange fest miteinander verbunden" (p. 339).

Like Gadow he believed that in all vertebrates —not excluding the tetrapods—there were at least embryonically two pairs of dorsal arches and two pairs of ventral arches per segment, but for tetrapods he founded this opinion on evidence or concepts rejected by Gadow—on the "Neugliederung der Wirbelsäule" of Remak (1851), on the intrasclerotomic fissure of von Ebner (1888), and on the "Doppelwirbel" of Goette (1897), as embryologically interpreted. There were indeed four pairs of arches but in Schauinsland's view they persisted in all tetrapods. Both the dorsal arches and the centra were in all tetrapods double in origin and morphologically fully comparable in all cases. Schauinsland made no mention of Gadow's complex terminology for vertebral centra in tetrapods, nor did he vouchsafe any discussion of Gadow's views of the very different composition of the centra of the Amniota, urodeles, and Anura. Gadow's views are for the most part passed over as though Schauinsland thought them valueless and not worth discussion.

3. It remained for the much later work of Johannes Piiper (1928), in his paper "On the Evolution of the Vertebral Column in Birds," to fuse the concepts of Gadow and of Schauinsland. Piiper's work is classic and has strongly influenced all subsequent embryological studies.

There is no question that the series of papers, of which Piiper's was the first, that emerged from MacBride's laboratory in England and were published in the *Philosophical Transactions of the Royal Society of London* have established models of thoroughness, detail, and beauty of presentation which gravely diminish the value of later papers which do not measure up to this superlative standard. It has been the descriptive excellence of Piiper's work, not surpassed even by its successors in its own series and not approached by any others, which has fastened on embryological literature the complex, overly elaborate interpretative scheme he devised. It was, in fact, the superb quality of his material, the fine differences in staining which he was able to observe, which prompted Piiper to interpret every staining difference as a morphological entity.

Piiper started, as had Schauinsland, with a very solid foundation in the fact of a transverse division of the sclerotome of amniotes into cranial and caudal halves—a division accomplished by the intrasclerotomic fissure of von Ebner. Piiper, however, also explicitly distinguished—without stating how—dorsal and ventral portions of the sclerotome halves; he thus arrived at a

roughly quadripartite division of the prechondral precursor of an amniote vertebra. For the elements of this quadripartite division he then adopted Gadow's terms.

If Piiper had done no more than this he would not have made a major contribution. But having devised a terminology for sclerotome parts he then found himself able to follow by means of staining and cell density differences the fate of these sclerotome parts in detail, to a degree no one before him had even attempted. Having set up a basically simple theoretical scheme, he then discovered that the facts made it complicated. His prechondral "arcualia" were sclerotome areas and never did become discrete cartilages, nor did they correspond precisely to any adult structures. Thus the neural arch was composite, arising partly from dorsal tissue of the caudal half of one sclerotome (= "basidorsal"), partly from dorsal tissue of the cranial half of the next succeeding sclerotome (= "interdorsal"). In the latter Piiper recognized two subareas: a "dorsal-interdorsal" which became the postzygapophysis of the neural arch; and the interdorsal proper, which furnished part of the neural arch pedicel, and also a posterior dorsal quadrant of the centrum. Both the centrum and the intervertebral element that he called an "intercentrum" were also composite. The centrum was particularly complex, involving dorsally the basal portions of "basidorsal" and "interdorsal" and ventrally comparable arcual elements–the ventral portion of the caudal sclerotome half of one segment ("basiventral") and the ventral portion of the cranial half of the sclerotome of the next succeeding segment ("interventral")–and in addition to these another element sui generis, a zone of concentrically arranged cells (the "perichordal tube"). Furthermore, the centrum was not only composite in terms of sclerotome origin; distinguishable histological zones were present within it, and to these Piiper gave the names, "pre-" and "opisthospondylous zones" and "vertebral ring." The "intercentrum" (really a haemapophysis, the equivalent in neck and trunk of chevrons) arose from both ventral portions of the sclerotome of one segment, but the intervertebral disc above it arose from just the ventral portion of the cranial half of a sclerotome, and from a differentiated portion of the perichordal tube.

In the end, therefore, Piiper's vertebral analysis, professing to be founded on Gadow's very simple scheme of four pairs of arcualia, became frighteningly complex (Fig. 2).

Apart from the elaborateness of the analysis Piiper's theory differed from Schauinsland's principally in two ways: (1) recognition of prechondral areas rather than discrete cartilage arches as equivalents of shark arcualia; (2) use of Gadow's terms for these presumed equivalents of arcualia. There is good reason to question whether either of these points of difference (neither wholly original) was an advance, but Piiper's revelation of the real complexity of the derivation of vertebrae from sclerotomal elements was a very real advance. Later workers have differed with him in matters of detail (in part because they have dealt with different animals), but all have accepted his demonstration of the complexity of vertebral structure in terms of sclerotome origin as the true developmental picture. Indeed, later authors have made the picture still more complicated, stating (e.g., Dawes, 1930; von Bochmann, 1937) that the zygapophysial joint always occurred *within the* "dorsal interdorsal" of Piiper's (Fig. 3).

> This results in a neural arch of marvelous complexity: the prezygapophyses formed by the interdorsal of segment A, the pedicel and lamina by the basidorsal of segment A, the postzygapophyses and sometimes part of the pedicel and lamina by the interdorsal of segment B.

However satisfactory at the descriptive level, Piiper's theory came into grave difficulties when phylogeny was considered and his complex vertebrae were compared with fossil types and the phyletic series which paleontologists had on excellent evidence based upon them. Piiper himself had rather cursorily attempted to relate his ideas to a phyletic scheme, but in this he was not successful. The equation of sclerotome quadrants with the parts of a temnospondylous vertebra produced only contradiction and confusion, decidedly not an intelligible picture. The intercentra of birds and reptiles, for example, were according to Piiper composite structures derived from two sclerotome-halves; the paleontological record, on the other hand, appeared to say that intercentra in reptiles were exactly equivalent to the hypocentra of temnospondylous Amphibia and *always* simple unit structures.

The contradictions here have been sufficiently radical that Piiper's version of vertebral mor-

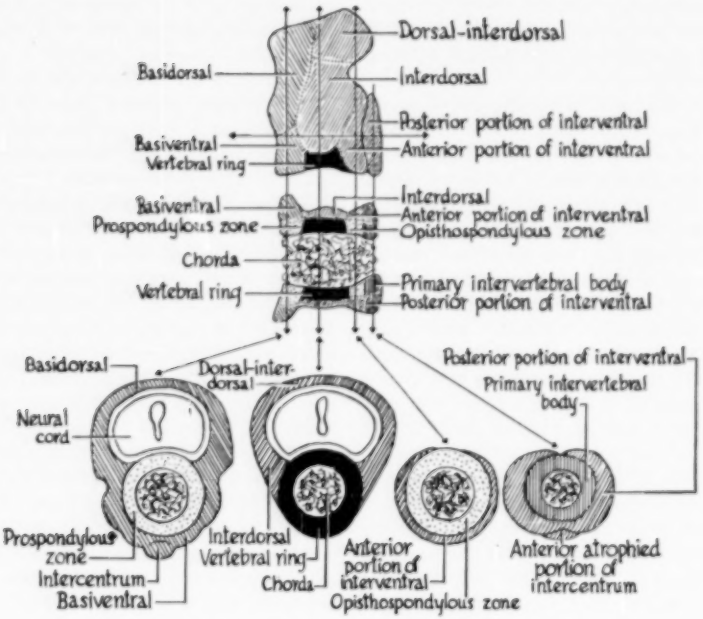

FIG. 2. PIPER'S ANALYSIS OF THE BIRD VERTEBRA

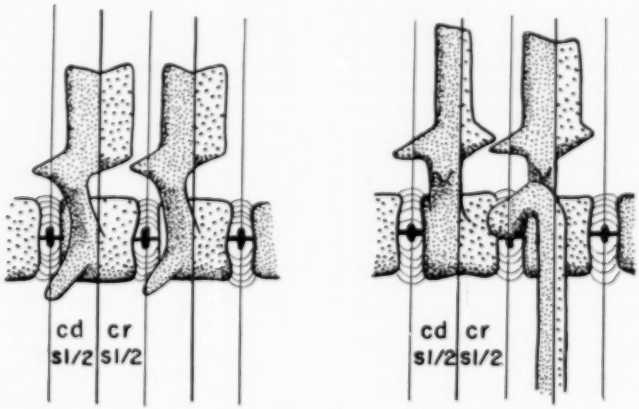

FIG. 3. ANALYSIS OF MAMMALIAN VERTEBRA AFTER VON BOCHMANN
cds½, caudal sclerotome half derivatives; *crs½*, cranial sclerotome half derivatives.

phology has frequently been ignored by paleontologists (for example, by von Huene, 1942, 1951) in favor of Gadow's theory of 1896. Though Gadow's theory was without real embryological basis it has appeared to square better with the paleontological facts. An embryologist, von Bochmann (1937), was so impressed by the difficulty of reconciling the phyletic and ontogenetic pictures that he explicitly denied that the two could be successfully compared. He stated: "Die Umbildung der Wirbel ist also nach jenem Typ phylogenetischer Entwicklung er-

folgt, den Sewertzoff Archallaxis genannt hat, es haben sich nicht nur die Endstadien geändert, sondern gleich die gesamten Entwicklungsvorgänge" (p. 52).

It is always possible, however, that the contradictions and difficulties lie rather in the theories than in fact. Let us now resummarize the embryological facts, in so far as possible, in neutral terms and rather than to impose upon them a general theory, let them build of themselves the needed generalizations.

THE DEVELOPMENT OF TETRAPOD VERTEBRAE

1. Amniotes

It is desirable to start a discussion of the development of tetrapod vertebrae with a summary of this process in amniotes. The best studies of vertebral development in tetrapods are of this group. To a great degree the nature of the material is responsible for this. The skeletogenous tissue is relatively voluminous, and the developmental process in no way abbreviated. Past confusions have been due almost entirely to the attachment of undue importance and false phylogenetic significance to transitory aggregations of cells that are merely preparatory or preliminary to definitive structures.

The development of vertebrae in the three classes of amniotes differs very little. Few of the differences recorded in the literature turn out on careful inspection to be more than differences in terminology and interpretation. Within classes contradictory assertions and reported divergences are even more often found to be grounded on such factors as differences in the ages of embryos examined.

In very brief summary, there are two stages in the ontogeny of the amniote vertebra: the stage of the sclerotome, and the stage of the vertebra. The first is a wholly preliminary, purely embryonic stage which is radically reorganized in its transformation into the second. The vertebra arises in place from parts of at least two successive sclerotomes and is laid down in precartilage with all its parts (except the neural spine) fully indicated from the first. It thereafter undergoes chondrification, ossification, and joint formation with only relatively minor differential growth or alteration of original relationships.

The description of amniote vertebral ontogeny below is a synthesis of the literature illuminated by special study of the Reptilia—the one group that in this aspect of morphology has been accorded insufficient attention in recent years. There has been no attempt to document every statement in detail but the following sources have been the most useful: von Ebner, Brünauer, and Männer for Squamata; Schauinsland, Howes and Swinnerton for *Sphenodon*; Higgins for crocodiles; Piiper for birds; and Dawes, von Bochmann, Reiter, and Sensenig for mammals.

My own studies on the development of vertebrae have been carried out principally on embryos of *Emys orbicularis* given me by Dr. B. W. Kunkel—some of the same embryos used by the latter in his own study (Kunkel, 1912) of the chondrocranium of this form. Only in this series was the study carried from precartilage to ossification stages. The sclerotome stages were examined in embryos of *Thamnophis sirtalis*, and later stages of this snake and of the lizards *Anniella* and *Eumeces* have provided some insight into the cartilage stages of the developing vertebrae of Squamata. These series were also given me by Dr. Kunkel. Material of *Lacerta* and of *Chrysemys* in the Minot Collection of Harvard University have also been examined to check conclusions reached on the basis of the series studied earlier. I have also had the benefit of an undergraduate thesis study of the development of the vertebrae in *Lacerta muralis* (especially caudal vertebrae) prepared under my direction by Mr. Robert Stanzler, then an undergraduate at Harvard University.

Stage I. The Sclerotome

The sclerotome in amniotes is notably rich in cells. When the ventromedial wall of the somite breaks down into mesenchymal cells and these migrate inward to surround nerve cord and notochord, the sclerotome forms a considerable mass of mesenchymal cells filling a wide area between dermatome-myotome and the nervous and chordal tissues. Successive sclerotomes are marked off from one another at this time by nearly cell-free transverse planes of separation—the intersclerotomic fissures (= intersomitic fissures, Piiper). Intersegmental blood vessels are closely associated with these intersclerotomic fissures and may mark their position long after the fissures themselves have disappeared.

Each sclerotome lies directly internal to the

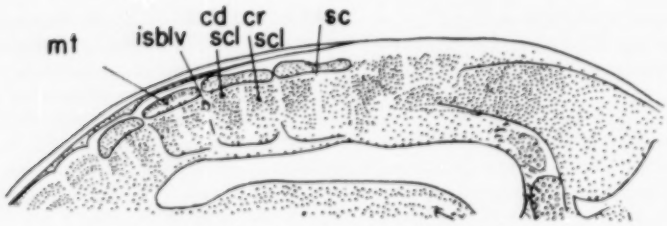

FIG. 4. SCLEROTOME AND SCLEROCOEL IN BIRDS (AFTER PIIPER)
Frontal section. *cdscl*, caudal sclerotome half; *crscl*, cranial sclerotome half; *isblv*, intersegmental blood vessels; *mt*, myotome; *sc*, sclerocoel.

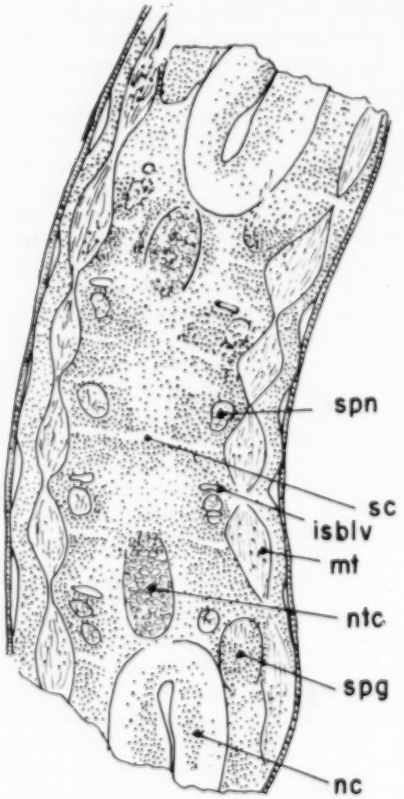

FIG. 5. SCLEROTOME AND SCLEROCOEL IN BIRDS (AFTER PIIPER)
Frontal section. *isblv*, intersegmental blood vessel; *mt*, myotome; *nc*, nerve cord; *ntc*, notochord; *sc*, sclerocoel; *spn*, spinal nerve.

myotome of its segment of origin, and neither sclerotome nor myotome at this earliest stage show any anteroposterior obliquity. Sclerotomal cells do not at this time extend dorsal to the nerve cord and may not initially surround the notochord completely. Within each sclerotome there is an internal, nearly cell-free transverse plane of division, the *sclerocoel* (Intervertebralspalte of von Ebner = fissure of von Ebner = intrasclerotomic fissure), which divides the sclerotome more or less completely into cranial and caudal halves (Figs. 4, 5).

The sclerocoel may, as it does in reptiles, have an original connection with the myocoel, or this connection, though well-marked at some period, may be secondary (as in birds, Schultze, 1896); or, as in mammals, the sclerocoel may first appear when the myocoel has disappeared or is hard to discern (Sensenig, 1949); or the connection may never occur (as in *Larus*, Piiper). At least in reptiles and mammals the sclerocoel is first clearly defined only laterally, but later it extends inward nearly to the nerve cord and notochord.

At first the sclerotome halves do not differ in density, but later in most (or all?) cases the caudal sclerotome half appears much denser and stains more darkly than the cranial sclerotome half. The cranial sclerotome half always contains the nerve roots and dorsal nerve ganglion.

Stage II. The Perichordal Tube

The first well-defined vertebral structure to appear is a condensation around the notochord in the region of the sclerocoel. On the anterior and posterior sides of the sclerocoel and medial to the sclerocoel immediately around the notochord, cells which were originally mesenchymal lose their processes and become crowded together in concentric rings, the perichordal rings (Fig. 6). These structures, which are sometimes called, because of their position approximately at the boundary between future vertebrae, "primitive intervertebral disks," show no segmentation in their innermost layers but laterally

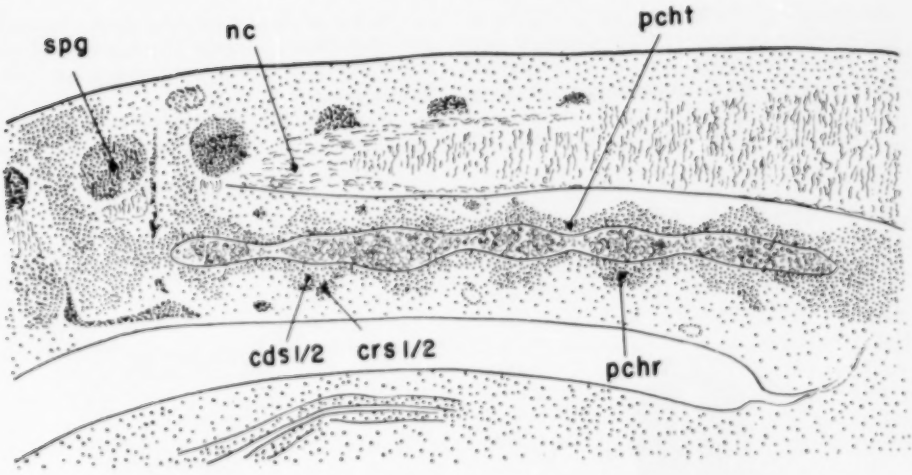

FIG. 6. PERICHORDAL RINGS AND PERICHORDAL TUBE IN BIRDS (AFTER PIPER)
Sagittal section. *cds½*, caudal sclerotome-half component of perichordal ring; *crs½*, cranial sclerotome half component of perichordal ring; *nc*, nerve cord; *pchr*, perichordal ring; *pcht*, perichordal tube; *spg*, spinal ganglion.

show their origin from two sclerotome halves of the same segment either by a cleft which marks the persisting sclerocoel or, with the eventual obliteration of the sclerocoel, by difference in the arrangement of the cells of the two components or by difference in the staining properties of the tissue from the two sclerotome halves. The amount of tissue contribution from each of the sclerotome halves seems to differ in the different forms.

Very soon after the formation of the perichordal rings the cells of the perichordal regions intervening between successive perichordal discs likewise lose their mesenchymal character. In the course of organization of these tissues, or somewhat before, the intersclerotomic fissures close, and the derivation of the cells of these, the future central areas, from the union of the caudal sclerotome half of one segment with the cranial sclerotome half of the next posterior segment is in later stages indicated approximately by the presence of the intersegmental blood vessels.

The innermost cells have now become concentrically arranged around the notochord, but the cells that become so arranged in this region are somewhat fewer than those in the intervertebrally placed perichordal rings. There thus forms a continuous axial tube of circumnotochordal cells of sclerotome origin, the *perichordal tube*.

Stage III. The Precartilage Vertebra

Until this point we are still very much in the stage of preliminaries without much that suggests or prefigures the ultimate vertebra. Now, however, the vertebra as a whole begins to be dimly outlined.

Condensations of greater or lesser density lateral to the nerve cord are now becoming defined; these are clearly rudiments of neural arches, their more compact basal portions representing the neural arch pedicels, their looser dorsal prolongations the neural arch laminae. The latter still do not quite reach to the dorsal-most level of the nerve cord, which is roofed over only by the loosest of mesenchyme (Fig. 7).

Most of each neural arch rudiment—its densest and best defined portion—lies between the transverse levels of the perichordal ring in front and the intersegmental blood vessels behind. This much of each arch therefore is derived from caudal sclerotome-half tissue. This principal portion of each neural arch, however, is united to its neighbors anteriorly and posteriorly by less defined condensations that overarch the nerve roots and dorsal ganglia and lie between the

intersegmental blood vessels in front and the perichordal ring behind. These dorsal connecting pieces are clearly cranial sclerotome-half derivatives and are the elements called the *dorso-intervertebrals* by Mookerjee (= dorsal interdorsal, Piiper = articular processes, Sensenig) (Fig. 8).

In birds (Piiper) cranial sclerotome-half tissue seems to contribute to pedicel and lamina in addition to forming the dorso-intervertebral; in turtles this appears not to be the case. In mammals there are varying reports in this regard (Sensenig, Bochmann).

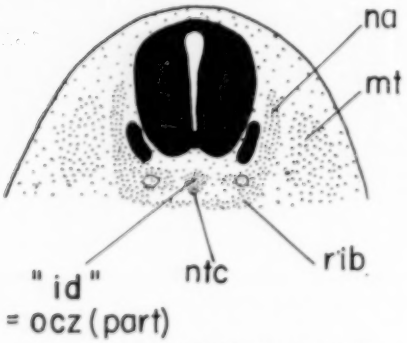

FIG. 7. PRECARTILAGE VERTEBRA OF *Mus* (AFTER DAWES)

Transverse section. "*id*," interdorsal Dawes; *mt*, myotome; *na*, neural arch; *ntc*, notochord; *ocz*, outer central zone.

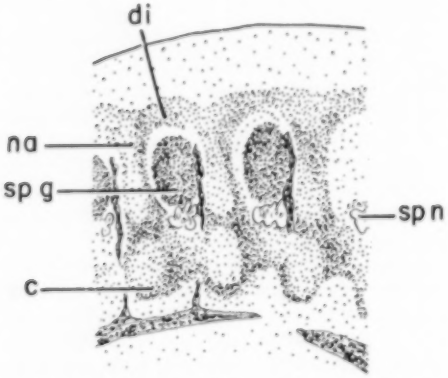

FIG. 8. PRECARTILAGE NEURAL ARCHES IN BIRDS (AFTER PIIPER)

Sagittal section. *c*, centrum; *di*, dorsointervertebral (= dorsointerdorsal Piiper); *na*, neural arch (= basidorsal Piiper); *spg*, spinal ganglion; *spn*, spinal nerve.

The line of contact between the neural arch pedicel rudiments and the vertebral zone of the perichordal tube is the neurocentral suture (Figs. 9, 10, 11).

The perichordal tube may still at this stage (*Sphenodon*, Fig. 9; *Alligator*, Fig. 10) be a

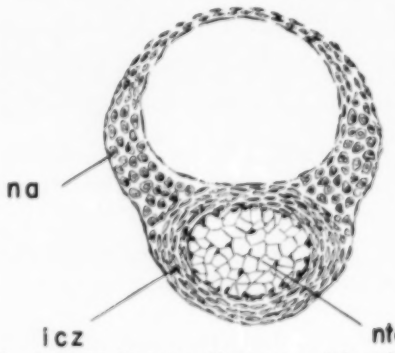

FIG. 9. EARLY CARTILAGE VERTEBRA IN *Sphenodon* (AFTER SCHAUINSLAND)

Transverse section. *icz*, inner central zone; *na*, neural arch; *ntc*, notochord.

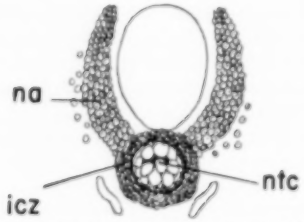

FIG. 10. PRECARTILAGE VERTEBRA OF *Alligator* (AFTER HIGGINS)

Transverse section. *icz*, inner central zone; *na*, neural arch; *ntc*, notochord.

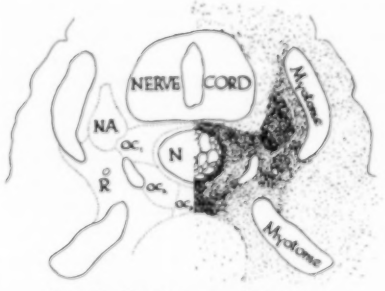

FIG. 11. PRECARTILAGE VERTEBRA OF *Emys orbicularis*

n, notochord; *na*, neural arch; oc_1, oc_2, oc_3, areas of outer control zone; *r*, rib.

simple area of concentric layers of cells closely packed around the notochord, or (turtles, Fig. 11; mammals, Fig. 7) there may be in addition to an *inner central zone* (= vertebral ring, Piiper) of cells retaining this concentric arrangement an *outer central zone* (= outer perichordal tube, Mookerjee) of more or less complex character. The cells of this outer central zone may show very different orientation and densities according to their positions at various levels around the notochord. It is not evident that the various areas within this zone have special morphological significance, though they have sometimes received special names (see below).

Within this outer central zone the cells lateral and lateroventral to the notochord are in turtles and mammals loose though no longer mesenchymal, and their arrangement with their nuclei tangential to an arc concentric with the notochord is only noticeable on close examination.

Midventral to the notochord, cells of this zone may be rather condensed; and a similar condensation exists middorsal to the notochord and is especially conspicuous in mammals (= "interdorsal," Dawes) (see Fig. 7). In turtles, but not in mammals, the areas adjacent to the neural arch pedicels consist of cell masses nearly as dense as the neural arch pedicels themselves; the same areas in mammals contain loose tissue.

At the stage in which these formations are seen in the vertebral region new organization has also taken place in the intervertebral region. The dense perichordal ring of the earliest stages has acquired or differentiated an equivalent of the outer central zone; the whole is now better called the *embryonic intervertebral disk*. Differences between inner and outer zones of this embryonic intervertebral disk are never so manifest as those between inner and outer central zones. Both zones of the intervertebral disk are very dense, and special differentiation of the outer zone is confined to its ventral portion, which may become histologically more advanced as a median ventral thickening. This is evidently the rudiment and equivalent of the ventral wedge-shaped elements called intercentra in living and fossil reptiles and in the lumbar region of certain mammals (e.g. moles).

From the ventral-most portion of the embryonic intervertebral disk additional condensations may be differentiated. These may be either paired or single and are closely attached ventrally to the ventral outer zone of the disk. These seem to be true ventral arch elements and to be the equivalent of the chevrons of the tail of adult amniotes, but they may, as in birds and *Sphenodon*, be present at this stage in all regions of the vertebral column. These elements may be conveniently distinguished from the intercentra and intervertebral disks as *haemapophyses*. Failure to distinguish these elements from the intercentra, with which they may be associated quite intimately in some forms, has been a source of confusion.

Intercentra seem in all forms to be derived, like the intervertebral disks themselves, from the tissue of the two sclerotome halves of one segment. Again like the intervertebral disks, the amount of tissue contributed by each of the sclerotome halves appears to vary from form to form.

The haemapophyses, however, though directly ventral to the intervertebral disks, seem to vary independently of them in regard to sclerotome-half derivation and may in at least some reptiles (Männer) and some mammals be wholly derived from cranial sclerotome-half tissues, or as in some birds (Piiper) be derived from tissues of both sclerotome-halves but principally from caudal sclerotome-half tissue.

Stage IV. The Cartilage Vertebra

The first differentiation of vertebrae began intervertebrally with the formation of the perichordal rings (= embryonic intervertebral disks). Chondrification is initiated in the vertebral region. There is a dispute as to whether cartilage formation begins in the neural arches or in the central region, but this probably varies from form to form.

In the neural arches chondrification begins in the region derived from the caudal half sclerotomes and may spread, perhaps with some delay, to the dorso-intervertebrals which were, as before mentioned, formed from cranial half sclerotome tissue, or there may be more or less distinct chondral centers in the dorso-intervertebrals. Continuity of all neural arch cartilage tends to be established for a period in later stages. Still later the zygapophysial joint breaks across the connection between successive arches (across the dorso-intervertebral). Whether this break is accomplished by connective tissue invasion (Mookerjee) or by lysis in situ is uncertain.

In the central region deposition of cartilage matrix begins in loose or relatively loose tissue of the outer central zone lateral and lateroventral to the notochord, and therefore appears first in the form of paired lateral centers. The loosening of tissue consequent upon the deposition of matrix may, as in *Sphenodon* (Fig. 12), be the first differentiation of an outer central zone. Chondrification then spreads to more condensed areas midventral and dorsolateral to the notochord, thus becoming a U-shaped center, and only as a relatively late phenomenon is the chondrification of the outer central zone completed by deposition of matrix in the condensed tissue dorsal to the notochord. The inner central zone of the perichordal tube is the last to become cartilage, and with its chondrification the cartilage centrum is completed.

Von Ebner (1892, p. 247) was the first to report that the centrum in amniotes chondrifies from two lateral centers formed initially in loose tissue. There is every reason to believe that this is the usual picture in amniotes. Contradictory statements may usually be charged to failure to observe the earliest stages of chondrification. Thus the observations of Männer (1899), who described the chondral center of the centrum as a U incomplete dorsally, and of Brünauer (1914), who described it as a complete ring, were based upon the same animal—*Natrix natrix*—that von Ebner principally studied, and their statements are therefore seen to be only reports of later and later stages of the same process of which von Ebner saw the inception. Similarly, the assertion of Dawes (1930) that the first central cartilage in *Mus* has the shape of a U except in the centrum of the axis where there are paired lateral centers may probably be attributed to a failure to catch the process of chondrification (except in the case of the axis) quite at its beginning. Bruni (1911), working with representatives of all the amniote classes, regarded chondrification of the centrum by paired centers in loose tissue as the rule. Sensenig (1948, 1949) strongly emphasizes the latter feature as a peculiar method of cartilage formation in mammals.

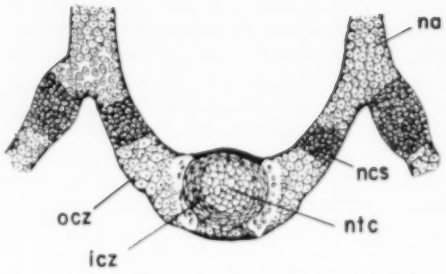

FIG. 13. LATE CARTILAGE VERTEBRA OF *Sphenodon* (AFTER SCHAUINSLAND)

Transverse section. Abbreviations as in Fig. 12.

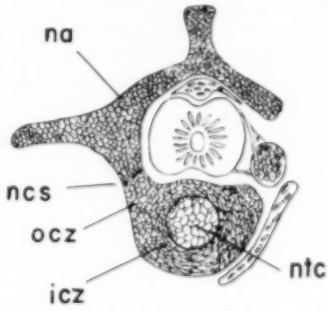

FIG. 14. LATE CARTILAGE VERTEBRA OF *Alligator* (AFTER HIGGINS)

Transverse section. Abbreviations as in Fig. 12.

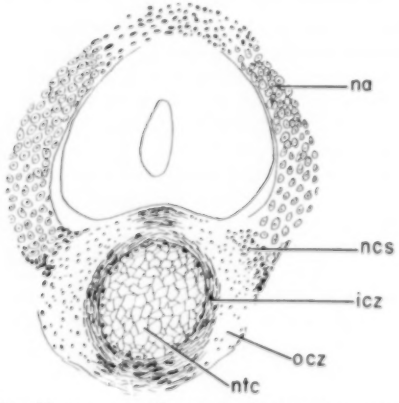

FIG. 12. ONSET OF CARTILAGE FORMATION IN THE VERTEBRA OF *Sphenodon* (AFTER HOWES AND SWINNERTON)

Transverse section. *icz*, inner central zone; *na*, neural arch; *ncs*, neurocentral suture; *ntc*, notochord; *ocz*, outer central zone.

With the completion of cartilage formation the neurocentral suture may be evident as a zone of closely packed small chondrocytes (Fig. 13, *Sphenodon*; Fig. 14, *Alligator*); or no such cartilage suture may ever be visible (birds, Piiper). This suture was already indicated in the pre-

chondral vertebra of *Emys* (Fig. 11) and is always clearly evident in cartilage stages in that form.

In this stage the completion of the neural arch above the nerve cord is accomplished. There may or may not be a subsidiary cartilage center in the neural spine (cf. various papers by Mookerjee).

The intervertebral disk lags behind in formation of cartilage, and in fact its tissue tends to be gradually assimilated in whole or principal part with the centra between which it lies. Any joint between successive centra is formed later by subdivision of the remnant of the original disk.

Stage V. The Bony Vertebra

With the end of the cartilage stage the architecture of the adult vertebra is well established. Ossification is primarily a process of replacement of the material of the cartilage model by more durable bone. According to Mookerjee, however, connective tissue ossifies directly both in front of and behind the chondral neural arches and is added to them as an important constituent of the adult arches.

In mammals a complicating feature is the presence of vertebral epiphyses. These are fundamentally portions of the embryonic intervertebral disk which have been added in cartilage to the centra but which ossify independently. The posterior epiphysis of one centrum plus the meniscus plus the anterior epiphysis of the next posterior centrum are the adult equivalents of one embryonic intervertebral disk.

2. *Amphibia*

It is not possible to describe vertebral development in the three orders of Amphibia in the same unified way as may easily be done for the three classes of amniotes. They have in the first instance been studied by relatively few authors with the same attention to detail as have the amniotes, and for the most part each order has been studied quite independently of the others and of the Amniota. Mookerjee (several papers) has most nearly succeeded in bringing them into proper frame of reference for comparison with the other tetrapods, but, very unfortunately, he has not studied the Apoda. There is thus no alternative but to describe vertebral development in each order separately. Fortunately, in all Amphibia vertebral development is shortened as compared with the process in amniotes, and it is consequently possible to be brief.

A. Urodeles

The material of the sclerotome is here considerably scantier than in amniotes. There is not nearly as much tissue to divide into cranial and caudal halves, and the evidence for such a division is weak. Fortman (1918) has described a sclerocoel in *Megalobatrachus*, but it is not a typical sclerocoel, as he freely admits. He calls it only an indication of or tendency toward one ("Andeutung oder Neigung").

Fortman's sclerocoel in *Megalobatrachus* is present before the release of the sclerotomic tissue from the scleromyotome and is a continuation of the myocoel into the forming sclerotomal tissue. In at least some sections the fissure (Spalte) expands into a cavity (Höhle). [See Fortman, 1918, pp. 127–128 and Figs. 1–3.] (In amniotes the sclerocoel is always a transverse fissure.) In *Megalobatrachus*, in contrast to amniotes, the sclerocoel disappears before the intersclerotomic fissures do.

Long before Fortman, Schauinsland called attention to Fig. 19 in Maurer (1906) (copied here as Fig 15). Maurer's figure shows in *Siredon pisciformis* a sclerotomal diverticulum containing an extension of the myocoel. Evidently the early development of the sclerotome in urodeles needs careful restudy.

Later stages in the ontogeny of urodele vertebrae have been well described only by Mookerjee. The following is a summary of his 1930 description:

As in amniotes the first structure to appear is the perichordal ring (= primitive intervertebral disk). As in amniotes, the disk is from its first appearance midsegmental—thus at the region at which a sclerocoel would occur were it typically developed.

The vertebral region marked off between the perichordal rings certainly includes tissue from two sclerotomes—the caudal part of one sclerotome uniting with the cranial part of the next posterior sclerotome. The neural arch pedicels arise opposite the posterior parts of the myotomes—thus from tissue that corresponds to the caudal sclerotome-halves of amniotes. Opposite the cranial parts of myotomes and lying above

nerve roots and dorsal ganglia are the dorsal connecting pieces between successive neural arches—the *dorso-intervertebrals* of Mookerjee (Schlussstücke, Fortman); these correspond in position and in tendency to delay in chondrification as compared with the neural arch pedicels to the similarly named cranial sclerotome-half derivatives in amniotes. As in amniotes the zygapophysial joint appears as a secondary break in these dorsal connecting pieces (according to Mookerjee, by connective tissue invasion). The spine of each neural arch is formed by a special cartilage piece.

In the perichordal region a perichordal tube develops between the perichordal rings. It is rather thin, consisting of concentric layers of mesenchymatous spindle-shaped cells, and never showing any distinction of outer and inner central zones; *it ossifies directly to become the centrum.*

According to Mookerjee, in the osseous stage the neural arch as preformed in cartilage is considerably extended both cranially and caudally by dermal bone.

Haemapophyses—ventral arch elements—when present lie directly under the main neural pieces, not underneath the intervertebral discs formed from the perichordal rings. Lateral processes of the ventral arches—parapophyses—may appear as such or as separate cartilage elements.

B. Apodans

All our knowledge of the development of vertebrae in this group derives from a paper by Marcus and Blume (1926) and another by Marcus (1937). Though the embryological observations in these papers are invaluable in the absence of any other, there are many peculiarities of conception and terminology which add to, rather than diminish, the (probably few) real

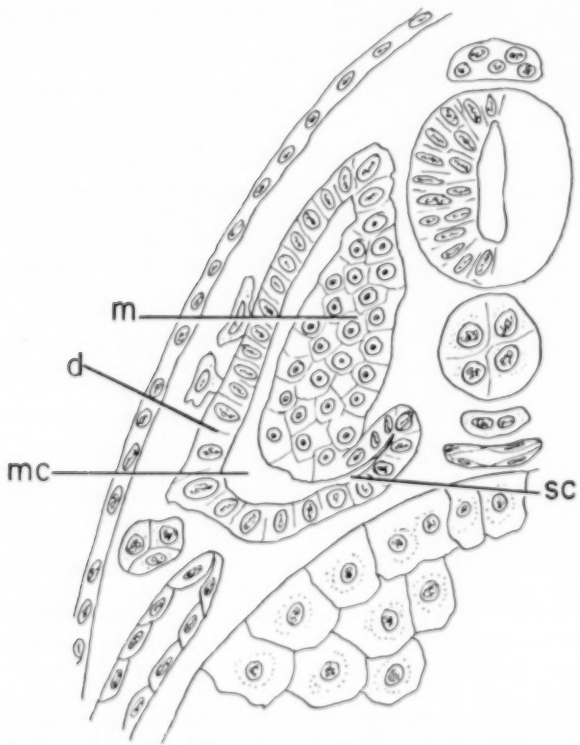

FIG. 15. SCLEROCOEL IN *Siredon* (AFTER MAURER)
d, dermatome; *m*, myotome; *mc*, myocoel; *sc*, sclerocoel.

difficulties of comparison with the Amniota and with the other Amphibia.

In some respects the Apoda are more like the Amniota than they are like the other Amphibia. The sclerotome is relatively rich in cells, and there is in the earliest stages a well-developed sclerocoel which is from the first in communication with the myocoel. The sclerocoel disappears before the intersclerotomic fissures do, but the cranial and caudal sclerotome-halves are persistently distinguished by differences in density as well as in time of histological differentiation.

The intervertebral disks form early, approximately midsegmentally, and persist throughout life. They are said to be formed only from cranial sclerotome-half material.

The main neural arch element is a caudal sclerotome-half derivative, but the connecting piece above the spinal nerve roots is formed from cranial sclerotome-half tissue and remains for a long time precartilaginous. Probably zygapophysial joint formation occurs within the connecting piece, but there is no explicit statement regarding this.

The central region is intersegmental in position and presumably formed from the tissue of the caudal sclerotome-half of one segment and the cranial sclerotome-half of the next succeeding segment. In precartilage stages there is only a rather thick perichordal tube without any evident differentiation into inner and outer central zones. In stages in which the dorsal arches are cartilaginous, the outer layers of the perichordal tube have been transformed directly into bone (much as in urodeles), but for a time a zone, possibly cartilage, a few cells thick exists between the bony ring and the sheath of the notochord (Marcus and Blume, p. 16, Fig. 45). The cartilage neural arches rest directly on the bony ring.

Very characteristically in Apoda there are anterior lateroventral processes of the centrum ("infrazygapophyses") which extend forward alongside the intervertebral region and the posterior part of the next anterior centrum. These are apparently ventral arch elements, and according to Marcus and Blume they are wholly cranial sclerotome-half derivatives.

There is an elaborate Rippenträger apparatus, as in urodeles, of which Marcus and Blume's "Parachordalia," prominently mentioned in the 1926 paper, are apparently part (Marcus, 1937).

C. Anurans

For Anura I principally follow Mookerjee (1930) and Mookerjee and Das (1935). In Anura a sclerocoel has not been recognized. Intervertebral disks are the first structures to form, and they form midsegmentally as in other tetrapods.

Dorsal arch rudiments arise opposite the caudal half of each myotome. These chondrify rather early. At a much later time precartilaginous rods (the dorso-intervertebrals of Mookerjee) connect the dorsal arches above the nerve roots and ganglia. These connections secondarily break apart (according to Mookerjee because of connective tissue invasion) and chondrify as pre- and post-zygapophyses.

The vertebral portion of the perichordal tube is well-developed but shows no differentiation into inner and outer central zones. The dorsal arches rest upon the perichordal tube and in fact appear impressed into it, so that the tube is thinner and more compressed dorsolaterally.

The further development of the central region proceeds according to one of two quite distinct patterns. In one the whole perichordal tube chondrifies, beginning underneath the arches, and this cartilage persists until replaced by bone. In the other either only the areas under the dorsal arches and that directly dorsal to the notochord chondrify, the remainder of the perichordal tube becoming fibrous, or a midventral portion of the tube also chondrifies at first but later degenerates into fibrous tissue. In the first pattern of development the resulting definitive centrum is "perichordal"; in the second the definitive centrum is wholly dorsal to the notochord, thus "epichordal" (Fig. 16).

Ventral arches are represented, according to Mookerjee, by the "hypocord," a median ventral element outside of and ventrai to the perichordal tube. This element, which is continuous longitudinally in the precartilage stage, becomes fibrous beneath the trunk vertebrae and only chondrifies and persists in the urostylar region. There it fuses with the centra, even in those cases of epichordal development in which the notochord and the ventral portions of the perichordal tube early degenerate.

The primitive intervertebral disks thicken and become cartilage (in forms with epichordal centra, only their dorsal portions). They are then the "intervertebral bodies" in which the intervertebral joints will (except in the Amphicoela)

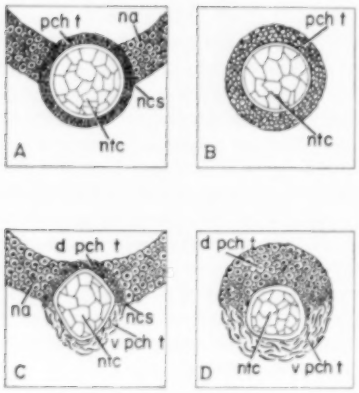

FIG. 16. CENTRA AND INTERVERTEBRAL BODIES IN ANURA (AFTER MOOKERJEE AND DAS)

Transverse sections. Perichordal type: A, centrum; B, intervertebral body. Epichordal type: C, centrum; D, intervertebral body. *d.pch.t.*, dorsal perichordal tube; *na*, neural arch; *ncs*, neurocentral suture; *ntc*, notochord; *pch.t.*, perichordal tube; *v.pch.t.*, ventral perichordal tube.

later arise by a secondary split (again according to Mookerjee by connective tissue invasion).

Ossification as usual replaces the model preformed in cartilage, but, according to Mookerjee, in anurans, as in urodeles, the neural arch is extended cranially and posteriorly by dorsal bone.

3. *Comparison of development in Amphibia and Amniota*

Comparing now the vertebral development in the Amphibia with the same process in the Amniota, several things are apparent.

There is no evidence that either centrum or arches in the living Amphibia differ at all in terms of sclerotome components from the similar structures in the Amniota. There is the same relation to primary segmentation in the two cases, and there is no indication of any shift of parts in the embryo or in later growth. *In all living Amphibia primitive intervertebral disks form early and approximately mid-segmentally, as in amniotes.* In all living Amphibia the neural arches appear to have two embryonic components, (1) a main portion—the pedicel and lamina, and (2) a dorsal portion arching over the spinal nerve roots. In this latter dorsal element the zygapophysial articulation arises. *The centra, though aberrant as compared with those of Amniota (in a somewhat different way in each of the orders) are intersegmental in place of origin as in amniotes and, again as in amniotes, are formed from perichordal tissue independently of the arches.* Thus in all its fundamentals vertebral development in the living Amphibia is very similar to that of amniotes.

The features in which amphibian vertebral development does differ from that of the Amniota fall into two categories:

(1) Features in which they show *obscurely* or *not at all* structures which are strongly expressed in the Amniota. The sclerocoel is such a feature in urodeles and the Anura.

(2) Features in which there is a striking *deviation* from the amniote pattern after some *initial resemblance*. The direct ossification of the centrum in urodeles and apodans and the epichordal centra in the Anura are such features.

None of these features, however, is fundamental enough or radical enough to count against the strong cross-resemblances.

REEVALUATION

We may now compare the facts of vertebral development, as we have seen them, with each of the classic theories—those of Gadow, Schauinsland, and Piiper—in turn.

GADOW: Upon critical reexamination, the Gadovian conceptions of the morphology of tetrapod vertebrae are found to have almost no relevance to the facts of tetrapod development.

1. *Thus there do not occur in tetrapods any such four discrete pairs of elements as Gadow imagined.*

Gadow's recognition of four pairs of arcualia in the Tetrapoda was in fact a forcing of observations into the mold of a preconceived theory. It was assumed, first of all, that there was some single plan for all vertebrae, whether those of tetrapods or of fishes. The vertebrae of fishes—in particular of sharks, since these were in Gadow's time considered *the* primitive fish—could be interpreted in terms of four pairs of arcualia. It was therefore deduced that tetrapod vertebrae should be thought of simply in terms of the fate of these primitive morphological entities—the four pairs of arcualia. In each case—in each class or order of tetrapods—only the original four pairs of elements needed to be accounted for, and the finding of these elements was a final and adequate solution of all the

morphological and evolutionary problems connected with the vertebrae in each class or order.

Gadow's line of thought is perhaps most transparently evident in his interpretation of urodele vertebrae. In this order Gadow could find only a single pair of elements in the neural arch and another single pair of elements forming the ventral arch. Clearly the first could only be the basidorsals and the second could only be the basiventrals. Where then were the interdorsals and interventrals? Gadow found these in the intervertebral cartilage. However, in most sections of embryonic vertebrae the latter appears to be a unit element without dorsal and ventral divisions. Gadow confesses this: "The formation of the intervertebral ring is accomplished rapidly; its constituent elements are not sharply marked." He hastens, however, to add that indications of a development of this element from four centers (first the dorsal ones, then the ventral ones) "appear now and then a little more clearly in long series of sections." All more recent authors (among them Schauinsland, Mookerjee, Smit, and Teege) have either failed to confirm this or are explicit in saying that it is untrue. Thus Mookerjee is very emphatic in saying that "there is no justification for saying that (the intervertebral cartilage) is derived from four cartilaginous centers."

Particularly clear here is the prior certainty on Gadow's part that the shark intercalary arches (interdorsals and intervertebrals) must be accounted for. The result was a zealous, and apparently overzealous, search for possible homologs.

An entirely similar zeal animated Gadow in dealing with other Tetrapoda. In each of these cases Gadow's zeal drove him to recognize homologs of shark arcualia in structures that were atypical in position and relationships or even in vague and evanescent aggregations of cells. Thus in birds and mammals he attached great importance to the "primitive Wirbelbogen."

The term "primitive Wirbelbogen" was first applied by Froriep (1883, 1886) to segmental mesenchymal condensations that are mere transitory differences in the density of sclerotomal tissues while in the process of transition to a more definitely organized precartilage state. Froriep's suggestion that these very temporary condensations were primitive vertebral arches and the precursors of the definitive vertebral arches has ever since been the occasion of dispute between those who place paramount importance on these structures and those who minimize them. The controversy between von Ebner (1888, 1892) and Corning (1891) involved this point as an important issue. Von Ebner flatly denied that these condensations were in any way related to the true arch anlagen; later opinion has sustained him. Gadow's reliance upon Froriep in this regard and his interpretation of the "primitive Wirbelbogen" as strict homologs not only of the definitive arches of the same form but also of the definitive arches of fish was thus another instance of unfortunate misinterpretation of vertebral development.

2. *There does occur the true resegmentation of the vertebral column that Gadow denied. In fact, no detail in the ontogeny of vertebrae is better documented than resegmentation in tetrapods.*

In amniotes the existence of a sclerocoel is now universally regarded as an established fact. It was first described in 1888 by von Ebner, in embryos of the common grass snake of Europe, *Natrix* (= *Tropidonotus*) *natrix*. Von Ebner found it as a result of a deliberate search for evidence for Remak's theory of the resegmentation of the vertebral column. He was the first to describe the original connection of sclerocoel and myocoel in snakes, and he, rather than Schultze (1896), is to be credited with the discovery of the secondary connection of the sclerocoel with the myocoel in birds (von Ebner, 1888, pp. 201–203 and fig. 6). Von Ebner also recorded a sclerocoel in lizard, mouse, and rabbit embryos. It has now been reported in *Natrix natrix* (von Ebner, 1888; Corning, 1891; Männer, 1899), *Anguis fragilis* (Corning, 1891; Männer, 1899), *Coronella laevis* (Männer, 1899), *Lacerta vivipara* (Corning, 1891; Männer, 1899), *Sphenodon* (Schauinsland, 1900, 1906), and *Emys orbicularis* (Eskin, 1929) among reptiles; in *Gallus* (von Ebner, 1888; L. J. Williams, 1942), *Diomeda* (Schauinsland, 1900, 1906), *Puffinus* (Schauinsland, 1900, 1905), and *Larus* (Piiper, 1928) among birds; and in *Mus* (von Ebner, 1888; Schultze, 1896; Dawes, 1930; Kamenoff, 1935; von Bochmann, 1937), *Rattus* (Weiss, 1901), *Peromyscus* (Sensenig, 1943), *Sus* (L. J. Williams, 1908), and *Homo* (Schultze, 1896; Bardeen, 1905; Reiter, 1942; Prader, 1947; Sensenig, 1949) among mammals. This is an incomplete list

mentioning only figured or well-studied forms.

Not only is the existence of a sclerocoel unequivocally demonstrated, but it is frequently possible, even after its closure, to find indications of its former presence such that the composite nature of such intervertebrally placed elements as haemapophyses can be conclusively shown. An excellent figure showing a ventral groove in the haemapophyses in the cervical region of a 14-day gull embryo is given by Piiper (his Fig. 12, here copied as Fig. 4). This groove quite certainly marks the point of union between cranial and caudal sclerotome-half components of these haemapophyses.

3. *There is no evidence of the fundamental difference in the morphology and segmental relationships of vertebrae between living Amphibia and Amniota that Gadow postulated.*

Two factors probably predisposed Gadow to an insistence on a fundamental difference between the modern Amphibia and Amniota: (a) a mistaken confidence in the position of ventral arches as accurate morphological markers; and (b) a failure to realize that centra in tetrapods as well as in sharks might be structures independent of the dorsal and ventral arches.

These two ideas reinforced one another, and (a very important point) seemed at the time that Gadow was writing to have a sound paleontological basis.

(a) In Amniota, at least in primitive members of all groups, the ventral arches (chevrons) of the tail lie *between* the centra. In modern Amphibia, whenever they are clearly to be seen (urodeles only) they are integral parts of the adult centrum. In Gadow's time this seemed to afford a clear presumption that the centrum (formed as it was supposed to be from vertebral arches) could not be homologous in the two cases.

When the fossil record was examined, the case for this interpretation appeared to be strengthened. In the early Amphibia of the large and important group Labyrinthodontia the primitive members have two centra per neural arch. To the anterior central element the ventral arch is always attached. In advanced members of the same group two strongly contrasting tendencies set in. In one group, which is on the fullest evidence considered ancestral to the Amniota, the central element carrying the ventral arch (the hypocentrum) tends to become reduced; in the other group—a branch destined to complete extinction—the centrum *not* carrying the ventral arch is reduced and ultimately disappears as an osseous element. For these two phyletic lines the fossil series is very full and convincing. The judgment that the two series culminate in forms with centra completely non-homologous, one compared with the other, is an exceptionally sound and secure one.

It had to be admitted, and was admitted in Gadow's time, that (as is still true) none of the modern Amphibia could be traced back satisfactorily to either of these phyletic series within the Labyrinthodontia. Nonetheless, the existence of these two series necessarily gave greater plausibility to the conception that the centra of modern Amphibia might well be morphologically very different from those of the Amniota.

Yet even in Gadow's period certain facts were known that might have occasioned caution in regard to a too-ready acceptance of this concept of non-homology. It is readily demonstrated within the living Squamata that the ventral arches do not have a fixed position and can be attached (in snakes, for example) without evident boundary to centra forward of their primitive intervertebral position.

This, of course, merely demonstrated the possibility of ventral arch shift; it did not demonstrate that it had occurred in the Amphibia. More pertinent and conclusive evidence came only with the modern detailed studies of vertebral ontogeny.

But these now seem to make clear that the *segmental position of the centrum, i.e., its relation to the primary segmentation of the modern Amphibia, is the same as that of the centrum of the modern Amniota* and that the *position of the intervertebral joint in the modern Amphibia is identical with that of the intervertebral joint of the Amniota.* This observation in itself goes to the heart of the question of the homology or non-homology of amniote and modern amphibian centra, but the modern embryological studies permit us to deal also with the problem which the difference in the position of the ventral arches in the modern Amphibia and Amniota presents; they show how a shift in position may have taken place.

On the one hand, in the Squamata the shift is a late ontogenetic phenomenon recapitulated in the life history of every individual. On the

other hand, the possibility of a more subtle shift not so obviously recapitulated is also indicated. The ventral arch in the Amniota (and presumably also, primitively at least, in the Amphibia) is the product of two sclerotome-halves of one segment. It has been shown, however, that in the Amniota the share of the two sclerotome-halves need not be the same. It is easily seen that if the cranial sclerotome-half contributes most of a haemapophysis, there may be a strong tendency for this ventral arch element to attach to the anterior of the two centra between which it lies.

(b) It was Gadow's viewpoint that, except in sharks, the centra of vertebrates were always formed from the bases of the dorsal and ventral arches; these "arch bases" were according to him the whole of the perichordal investment in higher forms. However, even before Gadow's first paper Goette had suggested that the primary vertebral centrum in amniotes (Primäre Wirbelkörper) was a formation quite independent of the arches. Much more recently Remane has strongly advocated the doctrine that centra are independent formations and has coined the term "autocentral."

Remane has specifically commented on Gadow's description of pseudocentrous, notocentrous, and gastrocentrous types of vertebrae in the Tetrapoda: "Diese Typenbildung leidet an zwei Fehlern. Sie lässt als Grundbestandteile nur die Bogenelemente gelten und leitet die Wirbelkörper lediglich von diesen ab; die Möglichkeit einer autozentralen Entstehung wird überhaupt nicht diskutiert. Dies ist um so bedenklicher als wir Interdorsalia und Interventralia nirgends mit Sicherheit bei den Tetrapoden nachweisen können, geschweige denn ihre Beteiligung am Wirbelkörper behaupten können. Eine autozentrale Entstehung der Körper ist aber nach den ontogenetischen Befunden kaum noch zu umgehen und damit wird die Bogentheorie der Wirbelkörperbildung vollends hinfällig."

Mookerjee, in a series of papers (a clear statement is in his address at the 1936 Indian Science Congress), has also insistently argued for the autocentral origin of the centrum throughout the Vertebrata. His studies have now resulted in a wider coverage and a better knowledge of vertebral development than anyone has had since Schauinsland. Except, however, for his first two papers in the *Philosophical Transactions*, his publications have been too brief and too incompletely documented to have had any effect on the vast inertia of scientific opinion.

The classic theory to which not only Gadow but also Schauinsland and Piiper have subscribed has the centra of all higher forms originating from so-called arch bases (Bogenbasen); both dorsal and ventral arches may participate, or only one or the other. Schauinsland and Piiper admit, however, the existence of a primary vertebral body that is truly autocentral. This is a zone of perichordally arranged cells at the core of the centrum. The independence of this zone is accepted by all recent authorities. There is added externally to this inner zone an outer central zone the cells of which may at some or at all stages lack any sort of boundary against the neural or ventral arches proper. Classically, continuity has been considered primary, any separation secondary or meaningless. The significance of this outer central zone is an important and difficult point. It will be discussed below, under the criticism of Piiper.

SCHAUINSLAND: Schauinsland's views were broadly based. He had in fact a wider knowledge of vertebral development based on personal investigation than any student has since attained (Mookerjee perhaps excepted), but this knowledge, though it included a far better comprehension of tetrapod vertebral ontogeny than Gadow's, was nowhere as intensive as it was extensive. There was therefore in Schauinsland's work a tendency to select certain striking facts and (without sufficient knowledge of their constancy or special meaning) to emphasize these above everything else, the more especially since these facts appeared to support a unifying theory applicable to all vertebrae in all vertebrates. Later studies call in question some of Schauinsland's most fundamental conclusions, and the comparisons and observations on which his basic theory depended now seem dubious.

1. *Thus there seems to be no simple way of comparing shark vertebrae and tetrapod vertebrae; there exists indeed a reasonable doubt that they are built to the same plan.*

The arches, whether dorsal or ventral, of chondrichthyean vertebrae are *space-filling elements that leave no portion of the nerve cord above, or of the caudal blood vessels below, exposed to lateral view.* This condition is possible only in cartilaginous fish, in which, even if cal-

cification is present, there is more elasticity than in bone. Such space-filling elements do not compare too precisely in their topographic relationships with the neural or ventral arches of other forms, in which there are always gaps above and below between the successive arches. It is in fact not obvious how the two kinds of elements are to be compared except in very general terms.

For Schauinsland, however, the two sets of arch elements per segment in the trunk region of cartilaginous fish seemed to fit so neatly with other scattered facts (the division of the sclerotomes in amniotes, the two neural arch struts per segment of *Petromyzon*) that the whole seemed to imply that there existed in both primitive and advanced forms something very like the double vertebrae (Doppelwirbel) that Goette had suggested as the basic pattern of vertebrae.

It has turned out, unfortunately, once a second look is taken at these similarities made so much of by Schauinsland, that the similarities were in many instances more verbal than substantial and often involve the glossing over of discrepancies.

In order to fit facts into the Doppelwirbel theory, in order to count in every case two sets of vertebral elements per segment, it was necessary (a) to consider as homologous even structures that are only vaguely similar or even really dissimilar, and (b) to treat as unimportant (or secondary) all instances of more than two sets of vertebral elements per segment.

(a) The intercalaria of sharks are typically structures that do not reach the level of the centra or touch this level only narrowly. The basalia on the other hand sit with broad bases upon the centra. Cells from the basalia are believed to invade the chordal sheath to initiate the formation of centra; there is, on the other hand, no evidence in typical sharks that the intercalaria participate in the formation of the centra at all. Yet when the comparisons are made between chondrostean and holostean vertebrae on one side and shark vertebrae on the other, the elements that are identified by Schauinsland and others as the homologues of shark intercalaria are *elements of the central region* and may in adult vertebrae become wholly embedded in the centrum. There would appear to be no ground for the suggested homology except the desire to count up to the correct number of elements per segment. Even so, an inspection of the classic figures of developing vertebrae of *Acipenser* (Fig. 17) shows that there are more elements in the central region than the Doppelwirbel theory can account for. Classically, the additional pair of elements has always been ignored as not fitting into the desired model of a vertebra.

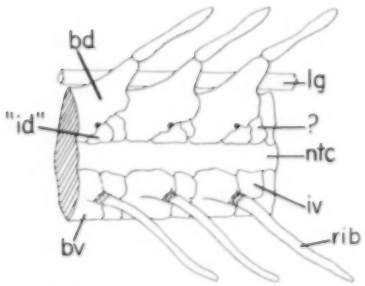

FIG. 17. *Acipenser*, PORTION OF VERTEBRAL COLUMN (AFTER GOODRICH)

bd, basidorsal; *bv*, basiventral; "*id*", "interdorsal"; *lg*, dorsal ligament; *ntc*, notochord; *?*, supernumerary element.

Even within the Chondrichthyes there is an ambiguity and uncertainty in Schauinsland's identification of the intercalaria vs. basalia. Compare his figs. 195, 200 with figs. 219, 220. In figs. 195, 200 (chimaeroids, *Callorhyncus*, *Chimaera*) Schauinsland identifies as *ob* (= oberen Bogen = basidorsals of authors) the elements that narrow ventrally and are pierced by foramina for dorsal nerve roots, and he also labels as ob_1 (= Interkalar-Stück = interdorsals of authors) the element with a broad base at notochordal level and pierced by the ventral nerve root. In figs. 219, 220 (typical sharks) he has reversed these identifications. It happens that in the preparations that Schauinsland studied the element that he identifies as *ob* is in each case the larger of the two elements; it would therefore appear that this is his real basis for decision, though as supporting evidence he claims that the intersegmental blood vessels (lying in each case just behind the "*ob*") support his identification. [However, according to his own figures, in sharks the intersegmental blood vessels may bend forward opposite the dorsal arches so that they have different positions relative to dorsal and ventral arches of the same area.]

It is noteworthy that Schauinsland never fully convinced Goodrich of the validity of his interpretation of the chimaeroid arches. In 1909 in the classic volume on the "Vertebrata Craniata"

in the Lankaster *Treatise* Goodrich labelled as interdorsal the element that Schauinsland had labelled "*ob*" and labelled as basidorsal the broad-based element that Schauinsland labelled ob_1. In 1933 Goodrich so far relented as to give the equivalents of Schauinsland's identification on his figure of chimaeroid vertebrae, but in each case with a query. The reader may form his own judgment. Figs. 18 and 19 compare shark and chimaeroid vertebrae labelled according to Schauinsland's scheme.

(b) The careful study by Rabinerson (1925) of polyspondyly in the tails of sharks and rays has led him to conclusions very different from those of Schauinsland in regard to these classic instances of multiple elements per segment. After close examination of polyspondyly in many forms, with figures of these conditions and of transitional regions of the column and of the many *irregular* conditions, so much more common than conservative opinion is aware of, Rabinerson questions the hypothesis of the secondary nature of polyspondyly and questions in particular the origin of this condition from two sets of arches per segment in the dorsal region. Rabinerson believes that both vertebral patterns in the cartilaginous fish—that of the trunk and that of the tail—have arisen from a stage in which *arch number per segment had not become fixed* and thus that as compared with this *indifferent* and *labile* stage the trunk vertebra is quite as much secondary and specialized as that of the tail.

Whatever may be the truth in these disputed matters, the significant fact is that the Schauinsland interpretations of chondrichthyean vertebrae are subject to highly plausible dispute. The Doppelwirbel hypothesis, which Goette founded and to which Schauinsland gave its classic statement, is far less securely based (even in its type case, the sharks) than many believe.

2. *There is no unequivocal evidence in tetrapods of morphologically meaningful doubling of neural or ventral arches in any post-sclerotome stage.*

Schauinsland, in attempting to apply the Doppelwirbel theory to tetrapods, placed reliance on five bits of evidence: (a) the double centra of primitive tetrapods; (b) the division of the sclerotome in the Amniota; (c) double arches in the tail of *Ambystoma*; (d) double arches in the tail of lizards; (e) staining differences in the cartilage vertebrae of birds.

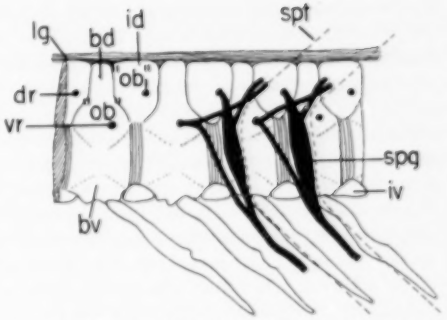

FIG. 18. *Squalus*, PORTION OF VERTEBRAL COLUMN (AFTER GOODRICH), TO SHOW SCHAUINSLAND'S IDENTIFICATION OF ARCH ELEMENTS IN SHARKS

bd, basidorsal; *bv*, basiventral; *dr*, dorsal root foramen; *id*, interdorsal; "*ob*", oberen Bogen Schauinsland, ob_1, Interkalar-Stück-Schauinsland; *spg*, spinal ganglion; *spt*, course of intersomitic septum; *vr*, ventral root foramen.

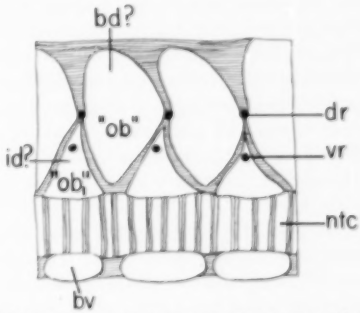

FIG. 19. *Chimaera*, PORTION OF VERTEBRAL COLUMN (AFTER GOODRICH), TO SHOW SCHAUINSLAND'S NOMENCLATURE IN CHIMAEROIDS

bd?, basidorsal?; *bv*, basiventral; *dr*, dorsal root foramen; *id?*, interdorsal?; *ntc*, notochord; "*ob*", oberen Bogen Schauinsland; ob_1, Interkalar-Stück Schauinsland; *vr*, ventral root foramen.

(a) The first of these bits of evidence is certainly valid, but its applicability in Schauinsland's sense disappears when it is realized that the central region is probably fundamentally independent of the arches.

(b) The division of the amniote sclerotome is certainly a reality also, but the sclerotome is a prevertebral structure. It is not comparable to anything in the definitive vertebra.

(c) The ascription of double arches to urodeles rests upon Schauinsland's figs. 284a and b of the tail of a 50 mm. *Siredon* larva. The evidence presented is that of a wax plate reconstruction; no histological sections are given. Doubled

caudal arches appear *not* to exist in the tail of *Salamandra* (Schauinsland's fig. 281a); and in *Siredon* Teege (1957) interprets appearances similar to those figured by Schauinsland in a quite different way: "Die kleinen caudal von einigen Neuralbogen gefundenen Knorpelstückchen im Schwanzgebiet von *Siredon mexicanum* stellen meiner Ansicht nach nur den Caudalteil der Neuralbogenbasis dar der die gelegentlich den hinter ihr abzweigenden Spinalnerven umwachsen kann." There is no hint of doubling of the neural arch in the adult vertebra of urodeles, and autotomy in salamanders is known to take place *between* vertebrae.

(d) Doubling of the neural arches in the tail of lizards and of *Sphenodon* is, on the other hand, a well-known and well-studied phenomenon. In both lizards and *Sphenodon*, separation of the neural arch into two parts has been demonstrated in the early cartilage stages of posterior tail vertebrae and is visible again in adult vertebrae of the same region, where it is associated with fracture planes that function in tail autotomy. It is probable that this condition is very strictly adaptive, since *even in the tail only those vertebrae that show fracture planes in the adult show doubling of the neural arch in the cartilage stages of vertebral ontogeny* (R. Stanzler, MS).

(e) Schauinsland's evidence for arch doubling in birds is given in his figs. 319 and 320 and concerns methylene blue preparations of cartilaginous cervical vertebrae. A staining difference has been interpreted as showing two cartilage centers in the neural arch. This also has never been verified. Piiper's much more elaborate study asserts the contrary, i.e., rather complete fusion in the cartilage stages of cranial and caudal sclerotomic portions of the neural arch (though there is division in the precartilage stages where it is a reminiscence of the primary segmentation).

PIIPER: Piiper's whole acquaintance with vertebral morphology was limited to the members (in fact, two members) of one class. His strength was his extraordinarily detailed knowledge of vertebral ontogeny in two genera of birds, his weakness a lack of knowledge and a very imperfect comprehension of the situation elsewhere. Thus there was on the one hand a tendency to overprecision in his identification of "structures" in his bird embryos, and on the other hand a contrary tendency to the greatest casualness and lack of precision in his phylogenetic suggestions.

1. *Piiper was very confident that the outer areas of the centrum were derived from dorsal and ventral arches but that confidence may well be based on a peculiarity of his special group. There is much evidence tending to show the "outer central zone" is autogenous, as Remane and Mookerjee have maintained.*

The conception that the amniote centrum is an arch centrum is an old and very persistent conception. Comparison of Figs. 9 and 13, of *Sphenodon*, and Figs. 10 and 14, of *Alligator*, shows the conditions that have led to the belief that the neurocentral suture in amniotes forms *within* an originally undivided neural arch and that amniote centra are at least in part formed by the bases of dorsal and ventral arches. The earlier (precartilage) stage in each case shows no indication of an outer central zone and no defined neural central suture, only a direct contact of neural arch and centrum, while in the later cartilage stage there is a clear outer central zone very distinct from the narrow inner zone of concentrically arranged cells and separated dorsolaterally by a well-defined zone of close-packed cells from the neural arch.

However, Fig. 3 of Howes and Swinnerton (1901), here reproduced as Fig. 15, makes it very plain that in *Sphenodon* the neurocentral suture of the late cartilage stages is in reality the same as the contact of neural arch and centrum in precartilage stages. The outer central zone is seen to be in the process of formation by a loosening of the outer cell layers of the centrum.

In *Emys* (Fig. 11) the outer central zone is already clearly indicated in precartilage stages, and there is never any possibility of considering the neurocentral suture secondary. With chondrification it merely becomes more clearly marked by the zone of closely packed small chondrocytes.

Mammals (Fig. 8) resemble *Emys* in this regard more than they do *Sphenodon* or *Alligator*. The outer central zone is present in precartilage stages. It is, however, represented by loose tissue, and the recognition of its significance has been complicated by the failure to realize that relatively loose tissue may be morphologically as much a "structure" as very dense tissue. Sensenig's discovery in 1948 of the origin of carti-

lage in loose tissue in the central region of mammals has clarified this point.

In modern Amphibia, the neurocentral suture is said to be absent. This is true, certainly, of the osseous *adult* vertebra in most instances, but there is a normal neurocentral suture in young *Liopelma hochstetteri*, as Dr. S. B. McDowell has shown me, and in all groups and forms there is in the embryo at some time or other some indication of a neurocentral suture. In Caudata and Apoda in which the centrum is formed directly in bone and the neural arch preformed in cartilage there is a sharp initial distinction which does not persist when the neural arch becomes ossified. In frogs the situation seems in reality to be very comparable to that in *Sphenodon*. Mookerjee's (1930) fig. 14, pl. 16 is very similar to the late cartilage stage in *Sphenodon* (Fig. 13, this paper) and may plausibly be interpreted in the same way—though no stage comparable to Howes and Swinnerton's figure of initiation of chondrification (Fig. 12, this paper) appears to be known.

It of course does not follow that the neurocentral suture as seen in subadult or adult *bony* vertebrae always represents the primitive zone of contact between neurapophysis and centrum. In reptiles, indeed, it probably corresponds rather closely to that original contact. The position of the suture when it can be determined in modern reptiles does not differ significantly from its position in the oldest fossil reptiles or in the seymouriamorphs, those equivocal creatures sometimes placed in the Amphibia and sometimes in the Reptilia.

The anomalous positions that the neurocentral suture may assume in mammals (Flower, 1885) are surely secondary. In many, perhaps most mammals, the neurocentral suture lies deep within the central mass; in whales it may, according to Flower (I have not been able to verify his observations), ascend on the neural arch so that a substantial fraction of this and even of the transverse process is ossified from the centrum (see Flower, p. 61 and fig. 20, repeated in Gadow and Remane).

We have here discussed the significance and origin of the "outer central zone" and neurocentral suture only for tetrapods, and here there are obscurities enough. But as Mookerjee has made very clear, an outer central zone exists also in fishes. In the latter—at least in certain stages—the outer central zone is clearly continuous with the neural and haemal arches. Hence the classical interpretation that the outer central zone is merely the bases of the arches—the Bogenbasen—is especially tenaciously held in regard to fish vertebrae. Mookerjee has, however, vigorously contested this opinion and has endeavored to show that in every case that he has investigated there is at some stage a separation or suture between the arches and the central areas just beneath or above them. He regards the outer central zone as autogenous in the whole series of vertebrates. I incline to Mookerjee's view, but I have not studied fish conditions, and it is only for tetrapods that I maintain the hypothesis of an autogenous centrum with full confidence. I would remark that no one believes that the so-called Bogenbasen in any group arise from anything but tissue in place, i.e, they are never literal outgrowths from the laminae of neural or haemal arches. They are therefore to this extent autogenous, and the dispute deals only with the importance attached to observations of continuity or separation.

For tetrapods I feel strongly that the fossil evidence (see further discussion below) and the ontogeny of such forms as the turtles and *Sphenodon* so fully insist on a fundamental distinction between neurapophysis and centrum that, with Remane, I regard the autogeny of the centrum as the only tenable hypothesis. That in the embryonic stages or the adults of certain forms, such as the birds studied by Piiper, the distinction between centrum and arch may not be evident is not for me a pertinent counter argument.

2. *Like his predecessors Piiper was guilty of a false equating of embryonic structures with adult structures in fossils.*

Piiper was even more naively Haeckelian than Gadow or Schauinsland. He first set up a series of ontogenetical stages and then proceeded to find every one of them represented in some adult ancestral type. Embryologically he distinguished (1) a *prespondylous stage*, essentially the stage of sclerotome-halves separated by a sclerocoel; (2) a *protospondylous stage*, in which perichordal rings first appear; (3) a *mesospondylous stage*, in which vertebral elements first become outlined in precartilage; and (4) a *metaspondylous stage*, in which the vertebra chondrifies.

He then continued:

> A comparison of the above-established ontogenetic stages with the vertebrae of different fossil and recent lower forms leads to the following suggestions: The prespondylous stage can be paralleled with the embolomerous type of vertebra occurring in fossil and recent Amioidei and some Carboniferous Stegocephalia. In the prespondylous as well as in the first period of the protospondylous, the vertebral centra bear a distinct arcogenous character and consist of distinctly expressed cranial and caudal half. The lower (= chordal) portion of the caudal sclerotomites is comparable with the anterior arch-bearing half of an embolomerous vertebra. The portion of the cranial sclerotomite disposed below the spinal ganglion can be compared with the caudal half of an embolomerous centrum.
>
> The protospondylous stage, where each sclerotome is differentiated into dorsal (= neural) and ventral (= chordal) divisions, which give rise to dorsal and ventral prechondral arcualia, presents a parallel to the more primitive forms of rhachitomous vertebra, which consists of 2 pairs of dorsal and 2 pairs of ventral arcualia (*Archegosaurus*). The membranous basidorsals with the dorsal interdorsals correspond to the neural arch, whilst the basiventrals can to a certain extent be compared with the hypocentra. The interdorsals find their equivalents in the dorsal pleurocentra and the interventrals in the ventral ones. It is probable that in fossil forms with temnospondylous vertebrae a layer of pliable tissue corresponding to the perichordal rings (resp. tube) was interposed between the osseous arcualia and the notochord.
>
> The mesospondylous stage, remarkable for the presence of the intercentra developed from the subchordal portions of the sclerotomes, can be compared with the type of vertebrae represented by certain Cotylosauria and Rhyncocephalia. The temporary and constant intercentra of *Larus* and *Struthio* are very likely homologous with the intercentra and chevron bones of the above-mentioned reptiles. . . .
>
> The metaspondylous stage, characterized by the absence of the trunk intercentra and by the amphicoelous form of the centra, vividly recalls the vertebrae of some mesozoic toothed birds, which are amphicoelous and devoid of intercentra. [Pp. 342–343.]

These phylogenetic speculations can only be described as worthless.

Thus Piiper's description of the prespondylous stage concentrates upon the central region for comparison with the embolomerous Amphibia, omitting any mention of the neural or ventral arches and therefore taking no notice of the fact (see Fig. 21, F) that these are as much single structures in embolomeres as in any other tetrapods. They are in fact indistinguishable from those of other tetrapods. But quite apart from this it is ludicrous to equate areas of not yet organized mesenchyme with articulating bony elements.

The protospondylous and mesospondylous stages, carefully examined, afford as little support to Piiper's thesis. If the protospondylous stage is comparable to the vertebrae of rhachitomous Amphibia, and if this is antecedent and ancestral to the mesospondylous and amniote condition, then there has been somewhere in the fossil series a most remarkable reconstruction of the central region in its transformation into the amniote centrum. The protospondylous centrum according to Piiper shows all of the central elements—hypocentra, pleurocentra, hypocentra pleuralia (the latter doubtfully alleged to be present in the rhachitomes *Archegosaurus* and *Chelydosaurus* and elsewhere unknown in adult tetrapods). In the mesospondylous stage these are all united in a single cartilage, and there appear as neomorphs unrelated to the hypocentra of rhachitomes the so-called "intercentra"—the haemapophyses of the present paper. When, however, we turn to the fossil record we find that ventral arches (= chevrons, haemapophyses) are always associated with hypocentra (in *Archegosaurus* as in all primitive tetrapods), that the association of hypocentra with haemapophyses is present in amniotes wherever, as in primitive forms, remnants of the hypocentra occur, and that the transition between the conditions in amniotes is bridged by a most complete series of intermediates. A reconstruction à la Piiper has never taken place. Furthermore, the rhachitomes such as *Archegosaurus* lie completely outside this phyletic series leading to the Amniota. Here again there has been a careless comparison of things not comparable—of precartilage areas and adult bony elements. It is small wonder that this sort of phylogeny-making (*a model of methods not to be used*) has caused confusion and dismay, and that embryologists since Piiper (e.g., von Bochmann) have found the paleontological evidence unintelligible, or that paleontologists (e.g., von Huene) have blithely ignored the more recent embryological

literature and have returned all the way to Gadow.

The fact is that Piiper has here discarded his usual rigor of method. He is frighteningly casual, ignoring the clear phyletic sequences that the paleontologist could set before him in favor of a hasty consultation of a few of the classic illustrations in paleontological texts, and even these he has taken at random, without regard to the true affinities of the forms compared and indeed without an appreciation of the total vertebral morphology in any of the cases chosen to be cited.

THE RESIDUE OF TRUTH

To demolish classic theories is not by itself a sufficient or a satisfying accomplishment. Descriptive detail without some guiding theory is a mere wilderness. We have now to ask what remains as a residue of truth after all criticism is done.

I have not promised a new synthesis, but I would be failing in my obligation to other students of vertebral development if I neglected to indicate the starting points from which, in my opinion, a new synthesis must proceed.

In my view, the division of a sclerotome into cranial and caudal parts by a sclerocoel is very probably a primitive embryonic feature at least as far back as the beginning of the tetrapods. The fact that this division, in addition to being universal in the Amniota, is clearly demonstrable in one of the three groups of modern Amphibia —the Apoda—speaks for this hypothesis. That the division is obscure or absent in the Caudata and Salientia is not an argument against it: the modern Amphibia are so unprimitive in most aspects of their morphology, they have lost or reduced or secondarily simplified so many structures, that simplification of a detail of ontogeny should cause no surprise. It is extremely likely that in the characters of the sclerotome, as in the adult skeleton, the Amniota are much closer to the primitive Paleozoic amphibians than are any of the surviving groups of Amphibia.

That a resegmentation of the vertebral column in roughly Remak's sense—a union of part of the caudal sclerotome-half of one segment with part of the cranial sclerotome-half of the next succeeding segment—is primitive for tetrapods may also be accepted without serious question. The sequence of change in vertebrae from the oldest Amphibia to the true Reptilia is so gradual that it is difficult or impossible to believe that the mode of origin of vertebrae in the modern Reptilia is not basically the same as the mode of origin of vertebrae in their Paleozoic ancestors. Likewise nothing in the abbreviated ontogeny of the modern Amphibia is contradictory of this point of view. The basic similarity of vertebral development, *especially the intersegmental position of the definitive centrum*, is impressive (see above, p. 16).

A qualification must be entered here. In the Amniota resegmentation in the sense described above is true for the bulk of the neural arch and for all of the pleurocentrum. It is not true for the prezygapophysial region of the neural arch or for the ventral arch or for the intervertebral disk (the homologue of the intercentrum = hypocentrum of ancient Amphibia). These latter are structures retaining the primary segmentation—arising from a union of tissues from the cranial and caudal sclerotomites of the same segment. Here again it is to be expected that what is true of the Amniota was true of the old Amphibia. An interpretation of the vertebrae of some of the Paleozoic Amphibia in terms of primary (sclerotome) segmentation appears in Fig. 20.

But primary segmentation is prevertebral; it merely provides the tissues from which definitive vertebrae arise. *If* primary segmentation really is expressed in the adult stage somewhere in the varied groups of modern fish, or if primary segmentation was at some time important in the adult vertebrae of the ancestors of the fish that gave rise to tetrapods, there has been at some unknown period a transformation such that in tetrapods and in the fish immediately ancestral to them the vertebra has been totally remade—*as it were, melted down and recast*.

The history of tetrapod vertebrae is to be understood quite simply in terms of the three separate elements that we find in the earliest Amphibia and in the fishes most closely related to them: the *neurapophysis*, the *pleurocentrum*, and the *hypocentrum* (with its associated ventral arch and rib). These are the only dramatis personae so far as the adult stage of any tetrapod is concerned. These three elements can be traced with perfect clarity via the Paleozoic anthracosaurs, embolomeres, and seymouriamorphs into the Reptilia and even into the mammals and

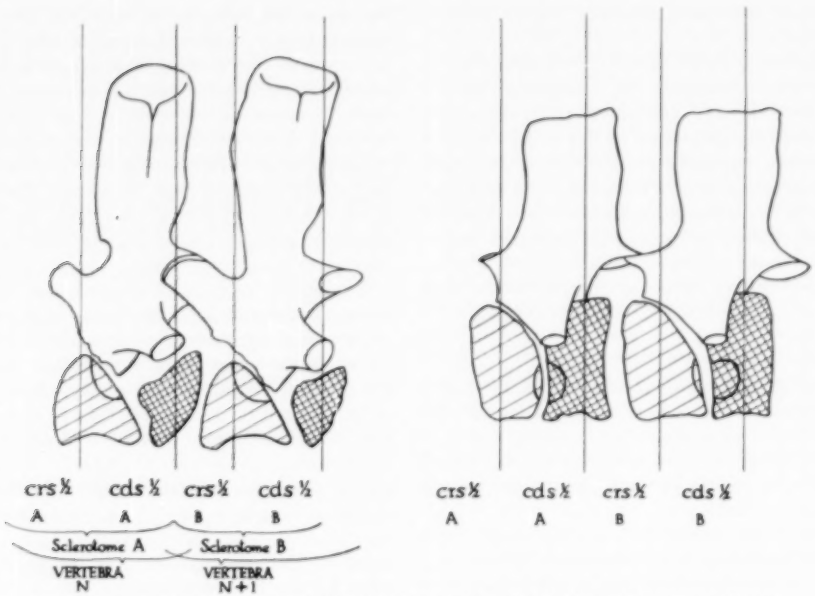

FIG. 20. VERTEBRAE OF ANCIENT AMPHIBIA INTERPRETED IN TERMS OF SCLEROTOME ORIGIN
Left: *Eryops* (after Romer). Right: *Archeria* (after Romer). *cds*½, caudal sclerotome half; *crs*½, cranial sclerotome half.

birds. In another wholly extinct phyletic line they can be traced from the Ichthyostegalia through the typical rhachitomes into the neorhachitomes and the culminating stereospondyls of the Triassic. These two lineages are perfectly clear and superbly documented. (Consult Romer, 1950, especially his phyletic tree on p. 306.) That embryological studies ever seemed to make these paleontological sequences difficult or obscure is due to a super-Haeckelian endeavor to find in ontogeny more than was there. It is the endeavor to find a shark vertebra somewhere within the developing vertebra of a tetrapod that has made a difficulty.

In both the two lineages thus far mentioned there is a conspicuous but gradual trend toward greater solidity in the region of the vertebral centrum. In the fish ancestors of tetrapods, as exemplified by the crossopterygian *Eusthenopteron*, all parts of the vertebra are less compactly and solidly constructed than in tetrapods, but the difference is greatest in the central region. In *Eusthenopteron* (W. K. Gregory, Rockwell, and Evans, 1939) the primary element of the central region was still the notochord, and the bony elements (2 sets per neural arch) were flimsy structures lying alongside (hypocentra) or dorsolateral to the notochordal sheath (pleurocentra) (Fig. 21, A). These structures could have provided very little strength and could have modified very little the primitive function of the notochord as an elastic rod acting as a unit. The situation was similar (Jarvik, 1952) in the oldest known tetrapods, the Ichthyostegalia of the upper Devonian—a group that in reality straddles the boundary between fish and land forms. In all later non-neotenic tetrapods, however, the notochord is essentially destroyed as a unit organ and is retained, if at all, as a cushioning element between a series of bony segments. In the two lineages already mentioned there are at first two bony centra for each neural arch. These centra are obviously derived from elements similar to those of *Eusthenopteron*. The same pleurocentra and hypocentra are present but have increased in thickness, compressing the notochord until it has only a narrow channel at the middle of each of the centra.

It is a striking fact that each of these two lines begins with the primitive condition of two cen-

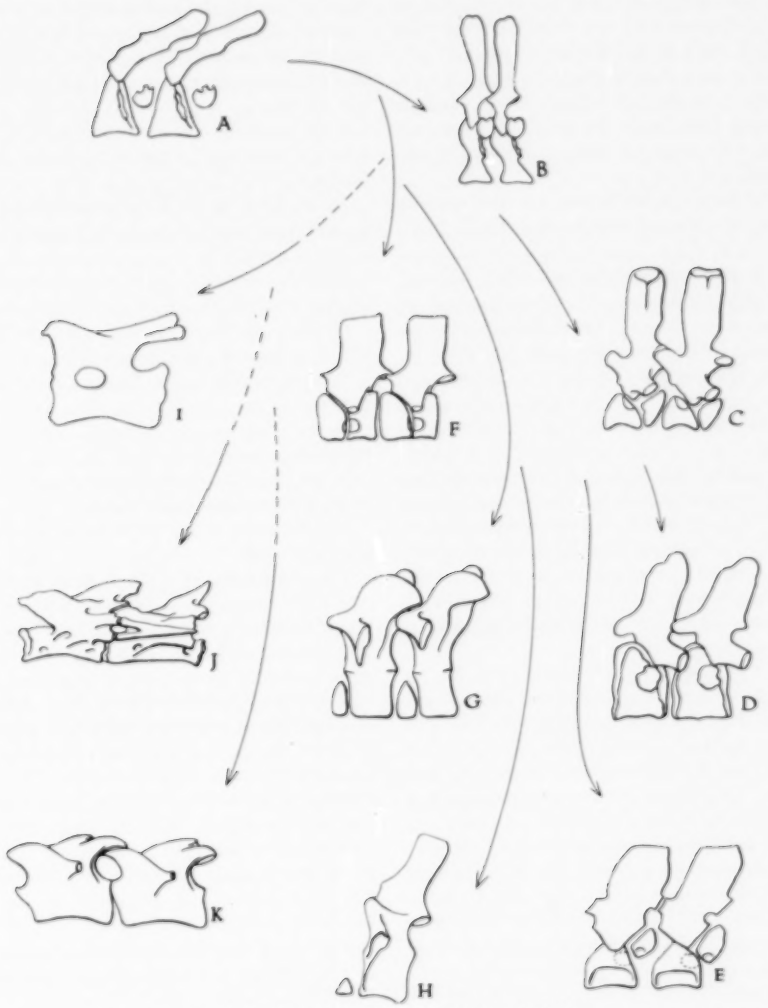

FIG. 21. THE PHYLOGENY OF VERTEBRAL TYPES

A, *Eusthenopteron*, the crossoptervgian stage; B, *Ichthyostega*, the ichthyostegid stage; C, *Eryops*, a rhachitome; D, *Mastodonosaurus*, a stereospondyl; E, *Lyriocephalus*, a trematosaurid; F, *Archeria*, an embolomere; G, *Seymouria*, a seymouriamorph; H, *Sphenodon*, the primitive amniote stage; I, *Cardiocephalus*, a lepospondyl; J, salamander; K, frog. A and B modified after Jarvik; C–H and J–K after Romer; I after Gregory, Peabody, and Price.

tra to a neural arch, but culminates in forms with only one centrum to a neural arch. In each the change is accomplished gradually. In each there is an experiment with two central elements approximately equal in size and which together, or with the aid of the neural arch bases, largely replace the notochord. The typical rhachitomes, such as *Eryops* with a double centrum of interlocking wedges (Fig. 21, C), represent such an experiment in one line; the embolomeres with their double centrum of two successive disks are the parallel experiment in the other line. In

neither lineage did the "two centra to a neural arch" experiment prosper; forms of this type either did not persist into the Triassic or persisted for only a short period. To judge by the event, the arrangement with a single centrum matched to and firmly united with its neural arch is by all odds the mechanically most efficient system.

Yet the single centrum was not the same in the two cases. In the line leading through the seymouriamorphs to reptiles the pleurocentrum prevailed, the hypocentrum persisting as a vestige or disappearing as an osseous element. In the other line—that of the rhachitomes which culminated in the stereospondyls—the hypocentrum was the surviving element, an arrangement which proved good enough to permit this group to survive through the first stage of the Age of Reptiles.

Thus far we have omitted one complicating bit of paleontological evidence. Among the earliest of tetrapods are the so-called lepospondyls, in which as a distinguishing feature of the group there are only two components to the vertebra—the neurapophysis and a simple spool-shaped centrum to which the ventral arch may be attached.

The lepospondyls appear abruptly in the fossil record. They are specialized and peculiar animals and most lines within this group have now surely disappeared without a trace. But they show in many aspects, and not least in the vertebral centrum, a similarity to salamanders and apodans, and speculation has often proposed that one or another group of lepospondyls has given rise to salamanders or apodans, or both. The gap between the modern forms and the Paleozoic ones is geologically wide; and direct demonstration that one is derived from the other does not exist. Nevertheless, since the structural gap is nothing like so large as the geological one, it is tempting to the point of inevitability to accept the suggestion of true affinity. (For a thorough discussion see Gregory, Peabody, and Price, 1956.)

We have made it clear above that the centrum of apodans and salamanders must, on the basis of intersegmental position, be regarded as a true or pleurocentrum strictly homologous with that of amniotes. If then we may reason from the vertebral morphology of the living forms to vertebral morphology in the ancient lepospondyls, we must regard the centrum of lepospondyls as a pleurocentrum and suppose that the hypocentrum had been reduced to at most a ligamentous or cartilaginous intervertebral pad between the osseous spools.

This point becomes very interesting if we now take a second look at the evolution of centra in tetrapods.

As we have seen, there were several experimental types of centra in the first period of tetrapod evolution:

(1) the primitive, relatively weak, fish-type double centrum found in the Ichthyostegalia;

(2) the interlocking-wedge double centrum found in the typical rhachitomes;

(3) the double-disk centrum of the embolomeres;

(4) hypocentrum-dominant double centrum of the neorhachitomes;

(5) pleurocentrum-dominant double centrum of the seymouriamorphs; and

(6) the single spool-like centrum of the lepospondyls.

The derivation of types 2, 3, 4, and 5 from type 1 is obvious: there is no ground for doubting that relationship. The lepospondyl condition is quite different. There are no known intermediates between type 6 and any of the others. Direct derivation from the ichthyostegalian type seems relatively difficult if we infer, as we have above, that the single element of the lepospondyls is a pleurocentrum. The pleurocentrum is far weaker than the hypocentrum in the Ichthyostegalia. Yet the lepospondyls are known to be among the oldest of Amphibia. They first appear in the early Mississippian. They are not as old, therefore, as the upper Devonian Ichthyostegalia but they are quite typical when they first appear—as typical in the centrum as in other features—and therefore pose a serious problem.

However, if the pleurocentral nature of the lepospondyl centrum is accepted, may not this be *prima facie* evidence of their relationship? The only other well-known groups of Paleozoic Amphibia with a pleurocentral centrum are the anthracosaur-seymouriamorphs and their aberrant offshoot the embolomeres. The transition from the ichthyostegalian double centrum to that found in these animals is a notable shift; in all this line the pleurocentrum is at least as large as the hypocentrum and usually larger. The

relationship with the Ichthyostegalia is evident only because of the persistence of the hypocentrum *as a bony element*. The shift in the anthracosaur-seymouriamorphs is in the same direction as that taken by the lepospondyls, it has merely gone less far, i.e., the anthracosaur-seymouriamorphs are more primitive.

Certainly the lepospondyls are not primitive. Quite apart from their central structure they show every sign of extreme specialization. They are among the first of tetrapods. Yet they are the first to reduce or lose the hard-won land limb. Many of them are quite limbless; all are with feeble limbs.

Since the lepospondyls are so specialized, they are most probably advanced representatives of one of the known more primitive patterns. The alternative is to suppose that they go back independently to a separate fish ancestry. The Scandinavians (e.g., Jarvik, 1955) do propose this solution, but it seems unnecessary, far-fetched, and chiefly based on convergent habitus resemblances.

If then the lepospondyls are to be derived from ichthyostegalians, rhachitomes, or anthracosaurs, the pleurocentral centrum speaks for anthracosaur affinities. I leave it to lepospondyl specialists to discover whether this hypothesis is contradicted by other aspects of their morphology.

One further problem regarding the lepospondyls may be mentioned: the question of selective reasons for their early adoption of a single centrum of the simple spool type. Two possibilities suggest themselves.

1. The lepospondyls differ from the remaining Paleozoic Amphibia in being small or snake-like or both. It may be inquired whether elongation and snake-like habitus requires more perfected functional relations between vertebrae than the stocky, less mobile habitus of the other types. It may be for such a reason that the trend

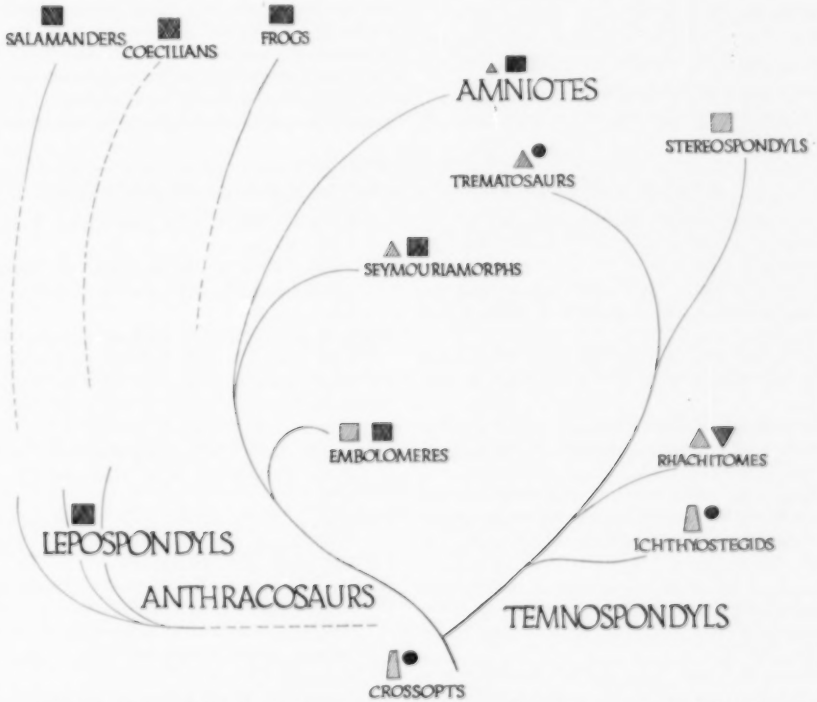

FIG. 22. A HYPOTHETICAL PHYLOGENY OF THE EARLY TETRAPODS BASED ON VERTEBRAL TYPES AS INTERPRETED IN THE PRESENT PAPER

Oblique lines, hypocentrum: cross-hatching, pleurocentrum.

to a single rather than a double centrum was earlier carried through in the lepospondyls than in the other Paleozoic Amphibia.

2. The lepospondyls are early specialized forms with loss of some bones in their skulls. If there is not an absolute loss of ossification there is certainly limitation and differential occurrence of ossification. May not the loss of the hypocentrum *as a bony element* be part of this trend?

We have not at any point in this discussion thus far mentioned the frogs. We have said nothing because there is nothing to say. The first veritable frog is relatively late (Triassic) in age; it provides us with no real clue to frog ancestry. With the destruction of Watson's hypothesis (1940) of the frog affinities of *Miobatrachus* = *Amphibamus* (J. T. Gregory, 1950), no alternative ancestor has been suggested. Again, the pleurocentral nature of the frog centrum suggests the anthracosaur-reptile lineage as at some point a source, but this suggestion is too imprecise to be very helpful.

Thus it is to be seen that I regard the tetrapods—especially the surviving ones—as exhibiting only minor modifications of a single pattern. The history of tetrapod vertebrae appears to me comparatively simple, once comparable stages are compared (Fig. 22).

I am doubtful whether similar simple sense can be made of fish vertebrae. The teleosts have proved very unfavorable for comparative study. New, very detailed investigations of vertebral development in the primitive bony fishes (*Polypterus, Amia, Lepisosteus, Acipenser*) and the Dipnoi are greatly needed, as well as new unbiased meticulous studies of the early stages of shark vertebrae and their sclerotomic antecedents. Currently the situation appears very confused—primarily, I believe, because of lack of facts. At all events, a new study will need an imaginative approach and one without rigid preconceptions of any kind. The facts must be fitted together, but they must not be *made* to fit, as it is my impression the "unifying" theories of the past attempted to do.

ACKNOWLEDGMENTS

The embryological studies which are the foundation of this review were begun under the direction of Dr. B. W. Kunkel. Discussions with Dr. A. S. Romer have been especially valuable. Prof. Bryan Patterson, Dr. Bobb Schaeffer, and numerous others have read the manuscript at some stage of preparation; their comments are gratefully acknowledged.

LIST OF LITERATURE

[Confined to cited papers; additional references in Remane and DeVillers]

Bardeen, C. R. 1905. The development of the thoracic vertebrae in man. *Amer. J. Anat.*, 4: 163–174.

Bochmann, G. von. 1937. Die Entwicklung der Säugetierwirbel der hinteren Körperregionen. *Morph. Jb.*, 79: 1–53.

Brünauer, E. 1910. Entwicklung der Wirbelsäule bei der Ringelnatter. *Arb. Inst. Wien*, 18: 133–156.

Bruni, A. C. 1911. Sullo sviluppo dei corpi vertebrali e delle loro articolazione negli Amnioti. *Arch. EntwMech. Org.*, 32: 89–167.

Corning, H. K. 1891. Über die sog. Neugliederung der Wirbelsäule und über das Schicksal der Urwirbelhöhle bei Reptilien. *Morph. Jb.*, 17: 611–622.

Dawes, B. 1930. The development of the vertebral column in mammals, as illustrated by its development in *Mus musculus*. *Phil. Trans.*, Ser. B, 218: 115–170.

DeVillers, C. 1954. Structure et evolution de la colonne vertebrale. *Traité de Zoologie*, 12: 605–672. Masson & Cie., Paris.

Ebner, V. von. 1888. Urwirbel und Neugliederung der Wirbelsäule. *S. B. Akad. Wiss. Wien*, Abt. 3, 97: 194–206.

——. 1892. Über die Beziehungen der Wirbel zu den Urwirbeln. *S. B. Akad. Wiss. Wien*, Abt. 3, 101: 235–260.

Eskin, I. A. 1929. Zur Entwicklung der Wirbelsäule der Sauropsida. 1. Zur Entwicklung der Wirbelsäule der Vögel. 2. Zur Entwicklung der Wirbelsäule der *Emys lutaria*. *Bull. Soc. Nat. Moscou*, N.S., 38 (Biol.): 284–356.

Flower, S. 1885. An introduction to the Osteology of the Mammalia. 373 pp. Third Edition. London.

Fortman, J. P. De Gaay. 1918. Entwicklung der Wirbelsäule bei *Megalobatrachus*. *Tijdschr. ned. dierk. Ver.*, 16: 121–167.

Froriep, A. 1883. Zur Entwickelungsgeschichte der Wirbelsäule, insbesondere des Atlas und Epistropheus und der Occipitalregion. I. Beobachtung an Hühnerembryonen. *Arch. Anat. Physiol.*, 1883, 177–234.

——. 1886. II. Beobachtung an Saugethierembryonen. *Arch. Anat. Physiol.*, 1886, 69–150.

Gadow, H. 1896. On the evolution of the verte-

—bral column of Amphibia and Amniota. *Phil. Trans.*, Ser. B., 187: 1–57.

——. 1933. The Evolution of the Vertebral Column. 356 pp. University Press, Cambridge.

——, and E. C. Abbott. 1895. On the evolution of the vertebral column of fishes. *Phil. Trans.*, Ser. B., 186: 163–221.

Goette, A. 1897. Ueber den Wirbelbau bei den Reptilien und einigen anderen Wirbelthieren. *Z. wiss. Zool.*, 62: 343–394.

Goodrich, E. S. 1909. Vertebrata Craniata. (First Fascicle: Cyclostomes and Fishes). In *A Treatise on Zoology* (R. Lankester, ed.), part IX, 518 pp. Adam and Charles Black, London.

——. 1930. Studies on the Structure and Development of Vertebrates. 837 pp. MacMillan & Co., London.

Gregory, J. T. 1950. Tetrapods of the Pennsylvanian nodules from Mazon Creek, Illinois. *Amer. J. Sci.*, 248: 833–873.

——, F. E. Peabody, and L. I. Price. 1956. Revision of the Gymnarthridae, American Permian microsaurs. *Peabody Mus. Bull.*, 10: x + 78 pp.

Gregory, W. K., Helen Rockwell, and F. G. Evans. 1939. Structure of the vertebral column in *Eusthenopteron foordi* Whiteaves. *J. Paleont.*, 13: 126–129.

Higgins, G. M. 1923. The development of the primitive reptilian vertebral column as shown by a study of *Alligator missippiensis*. *Amer. J. Anat.*, 31: 373–407.

Howes, G. B., and H. H. Swinnerton. 1909. Development of the skeleton of the tuatara, *Sphenodon punctatus*. *Trans. zool. Soc. Lond.*, 16: 1–76.

Von Huene, F. R. 1954. The principles of early tetrapod classification. *Amer. J. Sci.*, 252: 181–185.

Jarvik, E. 1952. On the fish-like tail in the ichthyostegid stegocephalians with descriptions of a new stegocephalian and a new crossopterygian from the Upper Devonian of East Greenland. *Medd. Grønland*, 114: 5–90.

——. 1955. The oldest tetrapods and their forerunners. *Sci. Monthly, Wash.*, 80: 141–154.

Kamenoff, R. J. 1935. Effects of the flexed-tailed gene on the development of the house mouse. *J. Morphol.*, 58: 117–152.

Kunkel, B. W. 1912. Development of the skull of *Emys lutaria*. *J. Morphol.*, 23: 693–780.

Macallister, A. 1893. Development and variation of the atlas. *J. Anat. Lond.*, 27: 519–542.

——. 1894. Development and variation of the second cervical vertebra. *J. Anat. Lond.*, 28: 257–268.

Manner, H. 1899. Beiträge zur Entwicklungsgeschichte der Wirbelsäule bei Reptilien. *Z. wiss. Zool.*, 66: 44–68.

tum und Rippen bei *Hypogeophis* und Urodelen. Beitrag zur Kenntnis der Gymnophionen. Nr. XXX. *Z. Anat. EntwGesch.*, 107: 531–552.

——, and W. Blume. 1926. Über Wirbel und Rippen bei *Hypogeophis* nebst Bemerkungen uber *Torpedo*. *Z. Anat. EntwGesch.*, 80: 1–78.

Maurer, F. 1904. Die Entwicklung des Muskelsystems und der elektrischen Organe. In *Handbuch der vergleichenden und experimentellen Entwicklungslehre der Wirbeltiere* (O. Hertwig, ed.), 3, part 1: 1–80.

Mookerjee, H. K. 1930. On the development of the vertebral column of Urodela. *Phil. Trans.*, Ser. B., 218: 415–446.

——. 1931. On the development of the vertebral column of Anura. *Phil. Trans.*, Ser. B., 219: 165–196.

——. 1936. The development of the vertebral column and its bearing on the study of organic evolution. *Proc. Indian Sci. Congr.*, 23: 317–343.

——, and S. K. Das. 1939. Further investigations on the vertebral column of Salientia. *J. Morphol.*, 64: 167–198.

Pieper, J. 1928. On the evolution of the vertebral column in birds, illustrated by its development in *Larus* and *Struthio*. *Phil. Trans.*, Ser. B., 216: 285–351.

Prader, A. 1947. Die frühembryonale Entwicklung der menschlichen Zwischenwirbelscheibe. *Acta anat.*, 3: 68–83.

Rabinerson, A. 1925. Beiträge zur vergleichende Anatomie der Wirbelsäule der Knorpelfische. *Anat. Anz.*, 59: 354–360, 60: 433–454, 481–495, 513–522, 560–565.

Reiter, A. 1942. Die Frühentwicklung der menschlichen Wirbelsäule. I Mitteilung. Die Frühentwicklung der Brustwirbelsäule. *Z. Anat. EntwGesch.*, 112: 185–200.

——. 1944. II Mitteilung. Die Entwicklung des Occipitalsegments und der Halswirbelsäule. *Z. Anat. EntwGesch.*, 113: 66–104.

Remane, A. 1936. Wirbelsäule und ihre Abkömmlinge. In *Handbuch der vergleichenden Anatomie der Wirbeltiere* (L. Bolk et al., eds.), 4: 1–206.

Romer, A. S. 1950. Review of the Labyrinthodontia. *Bull. Mus. comp. Zool. Harv.*, 99: 1–368.

Schauinsland, H. 1905. Die Entwicklung der Wirbelsäule nebst Rippen und Brustbein. In *Handbuch der vergleichenden und experimentellen Entwicklungslehre der Wirbeltiere* (O. Hertwig, ed.), 3, part 2: 339–572.

Schultze, O. 1896. Ueber embryonale und bleibende Segmentierung. *Verh. anat. Ges. Jena*, 10: 87–93.

SENSENIG, E. C. 1943. The origin of the vertebral column in the deer-mouse, *Peromyscus maniculatus rufinus*. *Anat. Rec.*, 86: 123–141.

——. 1948. Note on the formation of cartilage. *Anat. Rec.*, 100: 615–616.

——. 1949. The early development of the human vertebral column. *Contr. Embryol. Carnegie Inst. Wash.*, 33: 23–41.

——. 1957. The development of occipital and cervical segments and their associated structures in human embryos. *Contr. Embryol. Carnegie Inst. Wash.*, 36: 143–151.

SMIT, A. L. 1953. The ontogenesis of the vertebral column of *Xenopus laevis* (Daudin) with special reference to the segmentation of the metotic region of the skull. *Ann. Univ. Stellenbosch*, 29: 79–136.

TEEGE, M S. 1957. Studien zur Entwicklung und Gestalt der Urodelenwirbel. *Z. wiss. Zool.*, 160: 95–163.

WATSON, D. M. S. 1940. The origin of frogs. *Trans. roy. Soc. Edinb.*, 40: 195–231.

WEISS, A. 1961. Entwicklung der Wirbelsäule der weissen Ratte besonders der vordersten Halswirbel. *Z. wiss. Zool.*, 69: 492–532.

WILLIAMS, J. L. 1942. The development of the cervical vertebrae in the chick under normal and experimental conditions. *Amer. J. Anat.*, 71: 153–179.

WILLIAMS, L. W. 1910. The somites of the chick. *Amer. J. Anat.*, 11: 55–100.

——. 1908. The later development of the notochord in mammals. *Amer. J. Anat.*, 8: 251–284.

WYBURN, G. M. 1944. Observations on the development of the human vertebral column. *J. Anat. Lond.*, 78: 94–102.

COMPARATIVE GENETICS OF COMPLEX LOCI

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". . . if these d'Herelle bodies were really genes, fundamentally like our chromosome genes, they would give us an utterly new angle from which to attack the gene problem. They are filterable, to some extent isolable, can be handled in test-tubes, and their properties, as shown by their effects on the bacteria, can then be studied after treatment. It would be very rash to call these bodies genes, and yet at present we must confess that there is no distinction known between the genes and them. Hence we cannot categorically deny that perhaps we may be able to grind genes in a mortar and cook them in a beaker after all. Must we geneticists become bacteriologists, physiological chemists and physicists, simultaneously with being zoologists and botanists? Let us hope so."

H. J. MULLER, Dec. 29, 1921

ABSTRACT

Investigators of complex loci or pseudoalleles have attempted to analyze the structure and functions of the gene by the use of multiple allelic series. In the past decade a number of studies have presented stimulating findings and interpretations on the biochemical, topological, and physiological properties of genes. The historical background which led to these new discoveries is summarized and the basic problems involved are sketched. All of the present examples in Drosophila melanogaster *are individually considered for their unique features as well as their similarities. The problem of the universality of pseudoallelism is considered, with numerous examples of complexity in gene regions chosen from a wide variety of cellular forms. Special attention is also given to the interpretations of blood groups. In the microorganisms the contributions from viruses, bacteria, and the fungi are contrasted with the findings in the higher organisms. The major differences and basic similarities are pointed out in a comparative analysis of the various theories used to interpret the gene concept.*

INTRODUCTION

THIS REVIEW concerns the problems, findings, and interpretations of complex loci. Such a review, taken from the historical and comparative genetic point of view, becomes a history of the gene concept. This is unavoidable because the same problems which excite the interest of geneticists today provided the same stimulus for research to an earlier generation of geneticists—a stimulus which resulted in a body of knowledge indispensible for further investigation of these problems. Basically these problems may be stated in the following way: Is the genetic material in chromosomes continuous or discontinuous in organization? Are genes compound or single in structure? What is the relation between phenotype and genotype in terms of gene structure and function? What criteria are valid for defining the gene?

For the geneticist a comparative approach is a difficult task since his studies are usually limited to one organism, and hence there arises an inevitable development of a unique jargon and a superimposition of the genetic interpretations in that organism on the genetic findings in all other organisms. It is the author's hope that this comparative approach will point out some of the limitations of this habit of research. For example, people in different fields have associated somewhat different meanings with the words "gene," "locus," and "allele." In this paper the gene is given certain characteristics (see p. 59) which may be considered applicable primarily to *Drosophila*. In other organisms the characteristics of the gene show slight differences in structure from the Drosophila pattern and may be radically different on a functional level. Hence, rather than a precisely defined entity the term *gene* has become at present more of a

collective term, like the word *eye* (compare vertebrate, arthropod, and molluscan eyes, for example).

The use of the term *allele* is even more difficult to characterize, since it always remains a residual concept by the recombination test, which merely tells the geneticist that crossing over between alleles *has not yet occurred* for a specific number of progeny scored. In a broad sense, however, *allelism* may be considered the relation established by a series of mutants which show a mutant expression in the mutually heterozygous or compound situation with a deficiency for the genetic region being investigated. Usually these mutants are also allelic with one another, that is, they show a mutant expression in the compounds. On occasion they seem to act as non-alleles by showing a wild-type expression in compound. This phenomenon, called *complementation*, was well known to the multiple allelic series of *Drosophila melanogaster*. Its discovery in microorganisms by numerous investigators has led to some stimulating interpretations of gene function.

Finally, consider the use of the term *locus*. In its literal meaning it is only a mental construct; it was employed originally to refer to a point on a linkage map. More frequently it is used to designate a region of related genetic activity—a gene. This poses a problem, semantically, when recombination occurs within a complex locus or pseudoallelic region. The policy adopted here is to refer to the gene as a region or locus. The components of the gene which are separable by recombination occurs within a complex locus or *mutant sites*, depending, respectively, on whether one is referred to the gene concept, the linkage map, or the hypothetical molecule which composes this hereditary structure.

This paper will first consider some of the historical attempts at answering these basic problems of genetics. It will then describe the findings of pseudoallelism in *Drosophila melanogaster* and its influence on the interpretations of complex loci in other multicellular organisms. This exposition will be followed by a survey of the problems which have arisen with studies involving microorganisms. Finally, a comparative analysis of the various theories and findings, together with the major features of similarity and difference, will be presented.

HISTORICAL ASPECTS

As interpreted by Morgan and his colleagues, the gene was a stable molecule of small size located within the chromosome. Genes were separable from one another by recombination and were connected with one another by some bonding force or substance. On rare occasions the gene could mutate and its mutants were believed to be alterations of the gene molecule itself. These mutations were capable of reproducing themselves true to type.

In the early decades of genetics two schools of thought differed with this interpretation. In England, Bateson and his colleagues considered mutations as complete or partial losses of genetic material. This was called the "presence and absence" hypothesis. In series of multiple alleles, such as the white eye series in *Drosophila melanogaster*, the variety of mutant shades was interpreted as a series of deficiencies within the region varying from moderate (blood), to intermediate (apricot), to complete (white) absences of the gene. The "presence and absence" theory did not persist long, for several reasons. It provided no mechanism for the appearance of new genetic material for evolution. It made of evolutionary progress a continuous deterioration of the chromosome content. It failed to explain adequately the appearance of qualitatively new mutations. Most important, it could not account for the back mutations from the mutant to the wild type or normal—a process which was observed conclusively in *Drosophila* and supported in other organisms.

In the United States, Castle and his students, through an intensive investigation of the hooded character in rats, claimed that the gene itself was unstable and varied continuously, with selection not only directing the change in character, but also the corresponding changes in the gene. This variation in the gene he considered particularly effective in the heterozygous condition, where an allelic "contamination" might occur. Analysis of Castle's data by Muller showed that although the factor for hooded was controlled by a single gene, it was subject to modification by other genes. Several cases in *Drosophila* were analysed to illustrate this point, notably Beaded and Truncate wings. These all seemed to fit the theories of Johannsen and Nilsson-Ehle which considered multiple factor in-

heritance as the basis of quantitatively varying characters.

Thus, in the early twenties, it was possible for the Morgan group to formulate as follows a theory of the gene: "The theory states that the characters of the individual are referable to paired elements (genes) in the germinal material that are held together in a definite number of linkage groups; it states that the members of each pair of genes separate when the germ cells mature in accordance with Mendel's first law, and in consequence each germ cell comes to contain one set only; it states that the members belonging to different linkage groups assort independently in accordance with Mendel's second law; it states that an orderly interchange—crossing over—also takes place, at times, between the elements in corresponding linkage groups; and it states that the frequency of crossing over furnishes evidence of the linear order of the elements in each linkage group and of the relative position of the elements with respect to each other." (Morgan, 1926).

The theory of the gene provided an impetus for detailed analysis of gene action and structure. In the decade following, it enabled aberrant chromosome mechanisms and chromosomal rearrangements to be thoroughly investigated. Multiple allelic series came to reveal both a quantitative and qualitative complexity of the gene locus. As early as 1919, Muller recognized some of the problems raised by the complementation (appearance of the wild phenotype) of certain mutually heterozygous alleles of the dumpy series and rejected, for reasons as valid today as they were then, a one-to-one correspondence between the three phenotypic expressions and the three correspondingly linked adjacent genes which could have been proposed for them. "In such cases we may be dealing either with changes of different type occurring in the same material or with changes occurring in different component parts of one gene." (Muller, 1921).

Studies on mutation and mutation processes were considered invaluable in interpreting the structure and function of the gene. Thus a body of information was built up dealing with mosaicism, mutable genes, and temperature or other environmental and genetic effects on mutation frequency. By the late twenties, through the use of x-rays to induce mutations artificially, it was possible for Muller (1928) to assemble enough information to summarize as follows the status of the gene. First, the gene was extremely stable. Second, mutations were extremely localized, chance-determined, events and not ubiquitous chemical reactions involving the cell as a whole. Third, there was no evidence for a compound structure of the gene which would lead to a sorting out of mutant and non-mutant tissue somatically; nor would mutant and non-mutant offspring occur in later generations. Fourth, the entire spectrum of gene action encompassed visibles, lethals, semilethals, and detrimentals. Fifth, there was no difference in phenotype between point mutations of x-ray origin and those occurring spontaneously.

Another refinement in the theory of the gene was offered about this same time—the theory of step alleles. In the laboratory of Serebrovsky, where radiation analysis of *Drosophila* material was in progress, a series of mutations affecting the bristles and hairs of the thorax was discovered. These were similar to a mutation called scute, but differed from it and from each other by the number and kinds of bristles affected. At first it seemed that these mutants only expressed those bristle effects which were common to their allelic compounds. The remaining bristle effects were presumed to be mutually heterozygous, resulting in a complementary or wild-type expression. On this phenotypic basis, Dubinin (1933), Serebrovsky (1930), Agol (1931), and others constructed maps of the scute "basigene," as they called it, by using the complementation as a guide for the exclusion of the non-overlapping regions. This resulted in the division of the "basigene" scute into a continuous series of at least thirteen subgenes. The various scute mutants (step alleles or transgenes) affected one or more of these linearly arranged subgenes.

The theory of step-allelism was explicit in its consequences. "The results concerning the phenomenon of step allelomorphism lead us to very important conclusions in regard to the nature and structure of the gene. We first arrive at the conclusion that the gene is not, at least not always, something homogeneous, indivisible, but may be represented by a complex organisation, composed of separate districts joined with each other, each possessing its specific action. . . . If

the entire chromosome is continuous, that is, if one gene passes directly into another, then crossing over may pass only through the gene and not between genes, since step allelomorphism excludes any spaces between genes. . . . Normal allelomorphs differ from each other in the same degree as do their corresponding transgenes. The normal allelomorph of *scute*^{4} is not the same as that of *scute*^{3}, *scute* ^{2}, or *scute*^{1}. The latter all represent different regions in the normal chromosome." (Agol, 1931).

As beautiful as this theory was in the meticulous correspondence of each bristle or group of bristles to a single subgene, it soon collapsed from two independent sources of investigation. On a physiological basis, Sturtevant and Schultz (1931) and Child (1935) convincingly demonstrated the discontinuities in patterning which occurred when these same scute mutants were raised at different temperatures or were exposed to other environmental and genetic modifiers. On a genetic and cytological basis, Muller and Prokofyeva (1934), using the newly discovered salivary chromosome techniques and a careful breakage analysis, were able to demonstrate both minute and gross rearrangements in the yellow, achaete, scute region which limited the number of genes in that region to four or five.

In many ways the breakage analysis of the scute region by Muller and his colleagues represented the finest exploitation in *Drosophila* of techniques for revealing the continuous and discontinuous structure of the genetic material. (See review by Muller, 1956). The underlying principle of the technique assumed that if several independent rearrangements were obtained involving one break in or near the scute region and the other break in the heterochromatic region of the same arm of the X chromosome, then it would be possible, by recombination, to combine the left portion of one rearrangement with the right portion of another rearrangement (see Figure 1). Such a "left-right" technique would, if the breaks in the scute region were *not* in identical positions, reveal recombinant products showing a deficiency and a duplication for one

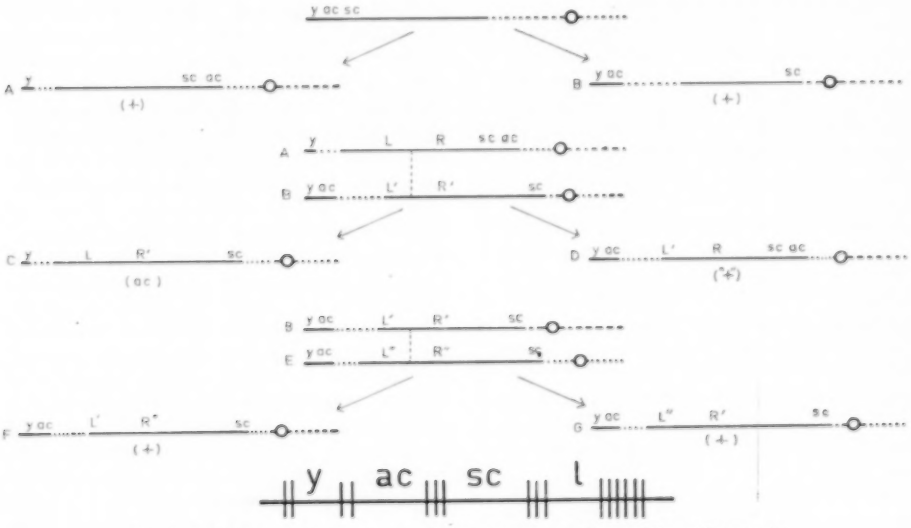

FIG. 1. BREAKAGE ANALYSIS OF THE SCUTE REGION IN *Drosophila melanogaster*

(A) and (B) represent two different rearrangements in similar regions. In the A/B compound, crossing over within the region results in a chromosome (C) deficient for achaete and a chromosome (D) carrying a duplication for achaete. If a third rearrangement, (E), is in compound with (B) and crossing over in the region produces no such deficiencies or duplications, then the breaks in that region are considered to be in the same place—intergenic. The "breakage map" for sixteen such rearrangements is illustrated to show discontinuity suggesting intergenic boundaries for the four traits involved. y, yellow body color; *ac*, achaete bristles; *sc*, scute bristles; *l*, lethal. L, R, L', R', etc., regions respectively to left and right of a specific chromosome break.

or more genes in that region. If the breaks were in the same place of the scute region (e.g., between the same pair of adjacent genes) then such a "left-right" test would show no difference between the recombinant parts and their original parts, since no excess or deficit of genetic material would result. In all, some sixteen rearrangements with breaks in or near the scute region were examined. If these were randomly distributed in a continuous genetic region, then most of them would reveal mutant expressions if the "left-right" test were performed, since even a small section of missing genetic material in this region would be expected to show a mutant effect. However, the analysis showed that these sixteen breaks were discontinuously distributed into five sites which bounded four distinct genes having separate phenotypes. If this evidence for the separateness of yellow, achaete, and scute, in the order demonstrated by the "left-right" technique, is valid, then a similar separation by crossover analysis should also be possible. An attempt to establish this was successful, with one probable crossover between yellow and achaete and four crossovers between achaete and scute (all in the expected directions according to the markers used), obtained from a total of about 75,000 flies (Dubinin, Sokolov, and Tiniakov, 1937).

An additional complexity was added to the gene concept when the phenomenon of position effect was discovered. Sturtevant (1925), working with the mutant Bar eyes, noticed that reversions of Bar to the normal round eye were always associated with crossing over. The striking fact that the homozygous Bar (B/B) showed a reduced eye and the recombinant double-Bar ($BB/++$) was even more extreme in its expression suggested to Sturtevant that a new genetic phenomenon, *position effect*, might be assumed to exist. Hence expressions of genes depended not only on mutations but also on the positions of the genes with respect to one another. As was later demonstrated cytologically by Muller et al. (1936) and by Bridges (1936), the basis for this position effect was a change in the relation of the Bar gene to its neighbors accomplished by a duplicated segment arising through an unequal crossing over in the region which contained the normal Bar gene. That a position effect itself, as Sturtevant had suggested in his original work, and not the dosage of normal Bar segments, was truly the mechanism for this mutant expression was demonstrated by Muller (1936) by comparing the four segments in the homozygous Bar female (which could be rewritten as $(B^+\ B^+/B^+\ B^+)$ with the compound $(B^+\ B^+\ B^+/B^+)$, consisting of the double-Bar chromosome (containing three such segments) and the wild chromosome (containing the single, unduplicated segment for the Bar region). The latter compound was found to be more extreme in phenotype than the homozygous Bar. Furthermore, when females heterozygous for Bar $(B^+\ B^+/B^+)$ are compared with females containing Bar in one chromosome and a deficiency for the Bar region in the other chromosome $(B^+\ B^+/Df\ (B^+))$, there is no difference in their appearance. Indeed, the deficiency for Bar shows no effect in compound with the normal chromosome. Later investigations by other geneticists revealed the existence of point mutations affecting the Bar mutant (with no accompanying visible rearrangements) and nonduplicational position effect Bar mutations of euchromatic (Baroid) or heterochromatic (B^{M1}) origin. Thus position effects assumed a more complicated relation to gene expression than was at first realized.

These complications in position effects rapidly accumulated, once x-rays were employed as a tool for obtaining gene rearrangement. Although Bar was a relatively stable mutant in its appearance, certain position effects showed considerable variegation or mosaicism in expression. Such variegated position effect mutations were usually associated with heterochromatin. The genes themselves, in either the stable or variegated types, were not permanently changed by their association with a new chromosomal or genetic environment, as was amply demonstrated by experiments of Dubinin and Sidorov (1934) and of Panshin (1935) for certain variegated mutants which could be crossed out of their affected sites into non-rearranged chromosomes and be thereby made to resume their normal functioning.

The developments in position effect analysis led to several theoretical interpretations of gene structure and action. One interpretation of position effect attributed the mutant expression to a distortion of the physical shape of the gene in the region of the break. The distorted gene molecule could thus not function in its normal capacity, and the altered products resulted in

abnormal phenotypes. A second interpretation considered the immediate genetic environment as essential to proper gene functioning. If a gene was separated from its neighboring loci its products could not interact with them, or would interact with foreign neighboring products, with the final gene products so altered that the mutant phenotype would result. (See review, Muller, 1935). With either interpretation of the mechanism of position effect, it was possible for Offermann (1935) to suggest that if a gene, *b*, were susceptible to position effect, then a mutation occurring in its left adjacent neighbor, *a* (which showed no visible effect of its own), could exert a position effect on *b*, resulting in a mutant expression of the unmutated *b*. Similarly, *c*, the gene immediately to the right of *b*, could likewise mutate (without a visible effect of its own) and cause a position effect on gene *b*. Finally, gene *b* itself could mutate as a point mutation involving neither *a* nor *c*. Thus in the sequence of genes *a-b-c*, mutation at either *a* or *b* or *c* could result in a mutant expression of *b*. This would lead to the paradoxical finding that a certain allele showing a (b) phenotype, in compound with another mutant of (b) phenotype, could give occasional crossing over or "reversion" to the wild type, and thus could lead to the establishment, by further use of this method of testing various mutants of (b) phenotype with one another, of three distinct positions for *b*. Note that this foreshadowing of pseudoallelism did not require that the neighboring genes in this "pseudoallelic" series show a homology, in the sense of a common duplicational origin, with the mutant actually responsible for the expression of the trait.

Indeed, this and similar considerations led Muller (1935) at first to ask whether all mutations might not be position effects forming a quantitative series from visible rearrangements to subvisible rearrangements. But the strong evidence for genetic discontinuity demonstrated by the "left-right" technique, and the properties of gene mutations and their causative agents, as well as the evolutionary demands for qualitatively new mutations led him to reject the application of position effect as a universal mechanism for mutation.

Goldschmidt, however, saw in position effect a mechanism that established a physiological model of gene action and structure. In a series of papers he (see review by Goldschmidt, 1955) urged the rejection of the concept of the discrete gene. In its place he proposed a continuous chromosome molecule in which alteration at any specific place would result in a specific mutant expression. In this model all mutations were position effects as a consequence of breaks interrupting or disarranging the normal chemical pattern of the chromosome molecule. In a manner analogous to that of Offermann's hypothesis, a series of alleles would be expected to show recombination with one another, since the chance that their breaks would be in exactly the same place must be extremely unlikely. This brings to mind the similar theory of step-allelism. The basic difference between the two hypotheses rests in the dependence of the theory of step-alleles on specific subgenes controlling specific functions, and the independence, in Goldschmidt's model, between the site affected and the agency for the function involved, since the entire chromosome itself would be the altered molecule and would produce the mutant effect.

One more chapter of interest in the history of the gene concept concerns certain fascinating studies of mutable loci. Some of these cases may be attributed to cytoplasmic inheritance, especially for plastid traits in photosynthetic plants. Some, as amply demonstrated in a number of cases in *Drosophila melanogaster*, could arise from heterochromatic position effects. The most interesting type, however, concerned three genes in *Drosophila virilis*—miniature-alpha, reddish-alpha, and magenta, affecting respectively the wing, eye color, and body color of the fly. In females heterozygous for the reddish-alpha trait there was a tendency for reversions to the wild type to take place in the reddish-alpha chromosome. These reversions occurred only during the maturation divisions and were not associated with recombination of outside markers or with gross chromosomal aberrations. In miniature-alpha three strains were obtained. The first, like reddish-alpha, gave only reversions during the maturation divisions; however, it could do so when the females were homozygous for this trait. A second strain showed mosaicism and reversions in the somatic tissue only and did not pass these reversion effects on to the progeny. It was therefore analogous to those heterochromatic position effects which were later observed in *D. melanogaster*. That these, however, could not

have been heterochromatic position effects (which were not known at that time) was demonstrated by Demerec (review, 1929) by means of a crossover analysis which localized the site of the miniature-alpha gene. Finally, a third type of homozygous miniature-alpha produced both somatic variegation and gametic segregation of these reversion types. Once a fly was obtained among the progeny which was wild type in appearance, it was stable.

Further investigations of these mutable lines by Demerec revealed the presence of a dominant gene (*S*) in an autosome which caused miniature-alpha to mutate somatically. Another dominant gene (*M*), also autosomal but not allelic to the somatic type, caused the miniature-alpha to revert germinally. Miniature-alpha was thus a true mutable gene, subject to modifying genes which could alter its rate and time of mutation.

That merely a complex structure of the gene strand was involved in the occurrence of mutation phenomena was demonstrated not to be so, as mentioned earlier, by Muller's first radiation experiments (Muller, 1929). For if mutation were to represent a sorting out of mutant and nonmutant components in a manner analogous to the way in which miniature-alpha sorted out reversions mosaically in somatic and germinal tissue, then a large number of fractional mutations should have been induced by x-rays. This was not the case. The majority of mutants obtained were whole-body effects which bred true, and no sorting out of mutant types occurred in the F_2 and F_3 inbred lines derived from these x-rayed lines.

The work on these mutable loci provided a stimulus for studies of gene complexity. The relation of such problems as "gene conversion" or other aberrant behavior in the segregation of alleles to these mutable loci is perhaps only coincidental. Exactly what made these *D. virilis* genes revert to wild type is still not known. That similar phenomena with other mechanisms exist will be shown in the sections on complex loci in organisms other than *Drosophila*.

Although many other investigations stand out in the early history of the gene concept, this survey would be seriously incomplete without reference to the stimulus which biochemical genetics received from the pioneering techniques developed by Beadle and Ephrussi in *D. melanogaster* (1936) and by Beadle and Tatum in *Neurospora* (1941). In a detailed study of eye pigments in *Drosophila*, it was possible to demonstrate diffusible substances which accumulated in the tissues of certain eye color mutants. With some biochemical knowledge of eye pigment formation, and an ingenious embryological technique, Beadle and Ephrussi succeeded in establishing which of the many eye color mutants participated in this particular synthesis and at what time in the sequence of events they acted.

Even more revealing, however, in the *Neurospora* studies, was the frequency of biochemical mutations, which seemed, for the most part, to affect the production of only one substance. This unique correspondence of a gene mutation to a specific biochemical impairment led Beadle and Tatum to formulate a "one gene—one enzyme" hypothesis in which each gene was functionally concerned with the production of a single enzyme which, in turn, acted on a specific biochemical substrate. When mutations impaired the production of the enzyme, utilization of the substance it acted upon also ceased, and the biochemical mutant could thereby be detected. Although many criticisms of this theory have been voiced, its stimulus to the field of microbial genetics has been immeasurable.

These historical theories and initial discoveries have recurred in altered form in the present decade. In the following sections we shall see how new techniques and increasing amounts of data from a variety of organisms have resulted in a series of competitive theories embracing physiological and unitary concepts of gene structure.

PSEUDOALLELISM IN DROSOPHILA MELANOGASTER

In 1940 an unexpected recombination, resulting in a reversion to wild type, occurred in a series of females heterozygous for some alleles of the lozenge eye series. At first, Oliver (1940), who discovered this phenomenon, could not detect the double mutant, but he did sample a number of cases which might have carried a double mutant chromosome. Neither these nor the recombinant wild types showed any peculiarities in the salivary chromosomes for this region. Another feature of this phenomenon, unlike the Bar eye case, was the consistent result of crossing over between these two alleles, as if one regularly lay to the right of the other. A similar report was made by Lewis (1941) concerning the mu-

tants Star and asteroid, with asteroid consistently crossing over as if located to the right of Star. The distinct difference in phenotype between the cis ($a_1a_2/++$) and trans ($a_1+/+a_2$) configurations of these mutants led Lewis to postulate a position effect relation which he believed had arisen through a duplicational origin of these genes. As evidence for this, Lewis observed in the salivary gland chromosome, the coincidental cytological presence of a doublet, or repeat, involving the region already known to determine the Star phenotype. Before proceeding with the theoretical aspects of pseudoallelism, however, it would be helpful to bring together the special features of each of the mutant series which have been investigated for this phenomenon.

Star Eyes (II, 1.3)

(Fig. 2)

In the Star-asteroid series (review, Lewis, 1945), two features are worth noting. First, the cis-trans difference introduces a phenotype not usually present in the expression of either of the other mutants alone. Star is a dominant rough eye mutant with recessive lethality. Its recessive allele, asteroid, is viable as a homozygote and shows a rough eye effect. In the trans arrangement, $S+/+$ *ast* shows not only a quantitatively exaggerated eye reduction and roughening, but also a disappearance of the distal portions of the wing veins. The mutants are resolved into two loci, *S* and *ast*, in the order written, with about 0.02% recombination between them. Lewis (1942) reported a salivary repeat for the region. Many interesting features are also to be found in the trans compounds of the various asteroid alleles or as homozygotes. Thus ast^2, a viable rough eye recessive mutant is female-sterile. It is also lethal in combination with *S*. The gaps in wing venation can also occur in some homozygous asteroid flies, although the expression is weak. Similarly the compounds ast/ast^2 and ast/ast^4 show an effect on wing venation. Apparently in these various combinations the effect on the eye and the wing are independent of one another in terms of the intensity of the effect expressed.

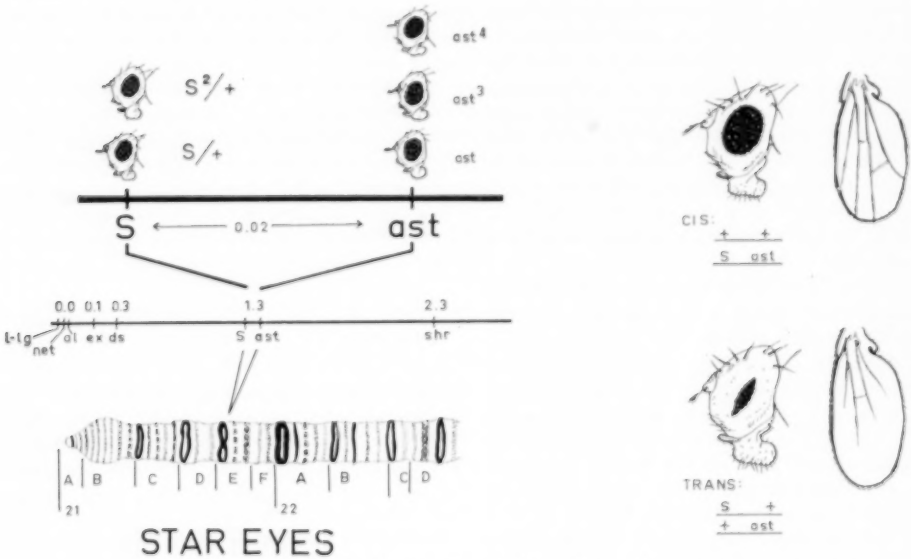

FIG. 2. STAR EYES IN *Drosophila melanogaster*

Left, genetic map of the left end of chromosome 2, based on recombination, and below, the corresponding portion of the salivary gland chromosome. Above each sublocus on the genetic map are arrayed the alleles known to be assignable to it. Right, comparison of effects in the cis and trans arrangements. Note the absence of wing veins in the trans but not in the cis configuration. *S*, Star eyes; *ast*, asteroid eyes. Marker genes: *l-lg*, lethal giant-larva, *net*, net venation; *al*, aristaless; *ex*, expanded wings; *ds*, dachsous legs and wings; *shr*, shrunken wings.

The second item of interest concerns the complex behavior of a duplication for the Star-asteroid region (Lewis, 1945). If the duplication contains two doses of *ast* it is normal, or nearly so, in all combinations with its homologous chromosome, whether the latter bears a deficiency for this region or contains Star. In fact, this hypomorphic activity of the asteroid mutants is seen in the compound (+ *ast*) (*S ast*)/+ *ast*, which is nearly normal. That a position effect influences this hypomorphic activity is demonstrated by the similar compound (*S ast*) (+ *ast*)/+ *ast*, which is more intense, showing an asteroid phenotype. The deficiency for the Star-asteroid region expresses, in its various compounds, phenotypes similar to that of the double mutant *S ast*. It is interesting too, that either the *Df* (S^{+} ast^{+}) or the double mutant *S ast* is less extreme in its interaction with other asteroid alleles than is *S* alone.

It should be emphasized that these duplications (and the deficiency) for the Star-asteroid region are cytologically detectable by salivary gland chromosome analysis. They differ, however, from the type of repeat or "doublet" suggested by Lewis as being responsible for the pseudoallelism at this locus. The usual "doublets" do not show unequal crossing over among the progeny, but such cytological duplications as those found in Bar eyes and in these special Star-asteroid regions do show unequal crossing over.

Stubble (*III*, 58.2)

(Fig. 3)

The pseudoallelic system for this region also involves dominant and recessive mutations (Lewis, 1951). The stubbloid recessives reduce the length, but increase the thickness of the thoracic bristles. Stubble itself is homozygous lethal, but in the compound *Sb*/+ it acts as a dominant showing the typical reduction in bristles. In homozygous stubbloid (*sbd*) there is also a reduction in wing size, but the effect is variable. The *sbd* +/+ *Sb* trans form shows a stronger bristle reduction than that of homozygous *sbd* or the *Sb*/+ compound. In the cis form, however, a very remarkable effect is observed. The compound *sbd Sb*/+ is wild type! The dominance of *Sb*, although not its recessive lethality, appears to be suppressed by the juxtaposition of the stubbloid mutant (Lewis, 1958). Examina-

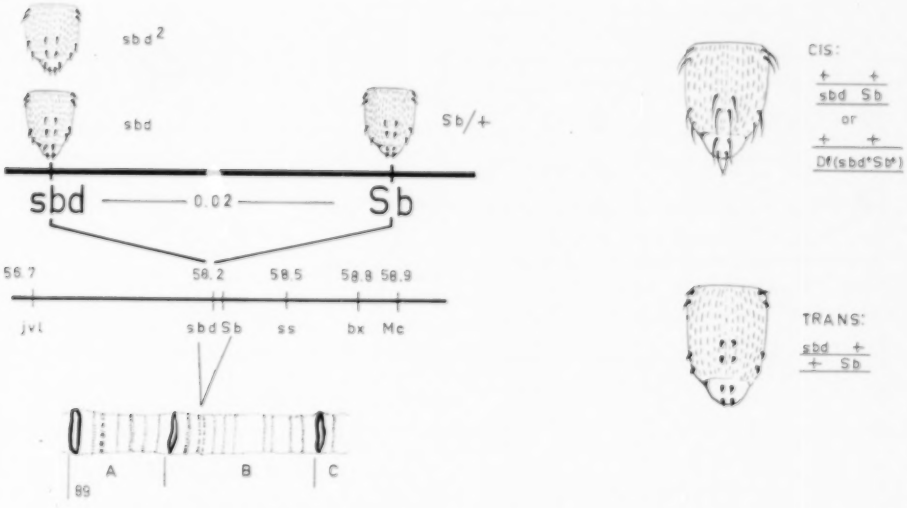

FIG. 3. STUBBLE BRISTLES IN *Drosophila melanogaster*

Sb, Stubble; *sbd*, stubbloid. Note the wild-type appearance of the bristles when the cis form is obtained; the dominance of Stubble seems to be suppressed by the presence of stubbloid. Marker genes: *jvl*, javelin-like bristles; *ss*, spineless bristles; *bx*, bithorax; *Mc*, Microcephala.

tion of a deficiency for the region shows that *Df* (*sbd*$^{+}$ *Sb*$^{+}$) behaves like the double mutant and does not show a dominance of the stubble phenotype. Although interactions for the wing effects have not been described in detail for the various stubble mutants, the semilethal *Sb*$^{sp^i}$ (Spike), in the form *Sb*$^{sp^i}$/+ shows a moderate bristle reduction and normal wings. But in trans association with *Sb* or as a homozygote, it shows the wing reduction and a strong stubble bristle effect (Dobzhansky, 1931).

It is interesting that both Star and Stubble, when coupled with their recessives, produce less extreme phenotypes than either mutant alone. This fact suggests, at first, a suppressor effect of the recessive subgene on the dominant subgene (Lewis, 1952; Pontecorvo, 1958). However, one aspect should not be overlooked—in both cases cytological deficiencies for the entire region result in phenotypes similar to, if not indistinguishable from, these double mutants. For this reason there may not be a specific suppressor activity of one subgene on another subgene, but an inactivation of the entire region achieved by bringing the two mutant subloci together. A genetic region with two alterations would not be likely to function as well as such a region with only one alteration in it. Hence, if a mutant acts as a dominant by producing a novel function for the gene, the function would probably be altered by bringing in another alteration which further changes the product produced by this region. For recessive genes, on the other hand, this problem does not arise, since double mutants would tend to reduce the efficiency of function of the region to a level equivalent to that of a cytological deficiency for the region itself.

Lozenge Eyes (X, 27.7)

(Fig. 4)

One of the most completely analyzed pseudoallelic series in *Drosophila* is the lozenge eye series. Phenotypically, Green and Green (1956) have distinguished three groups: *class I*, a moderately reduced rough eye with evenly distributed red pigment, female sterile; *class II*, a sharply reduced, smooth eye with marginal pigmentation, female sterile; *class III*, a sharply reduced, smooth eye with evenly distributed pigment, fertile. The sterility is associated with an absence of spermathecae and parovariae. An additional pleiotropic effect can be observed in the

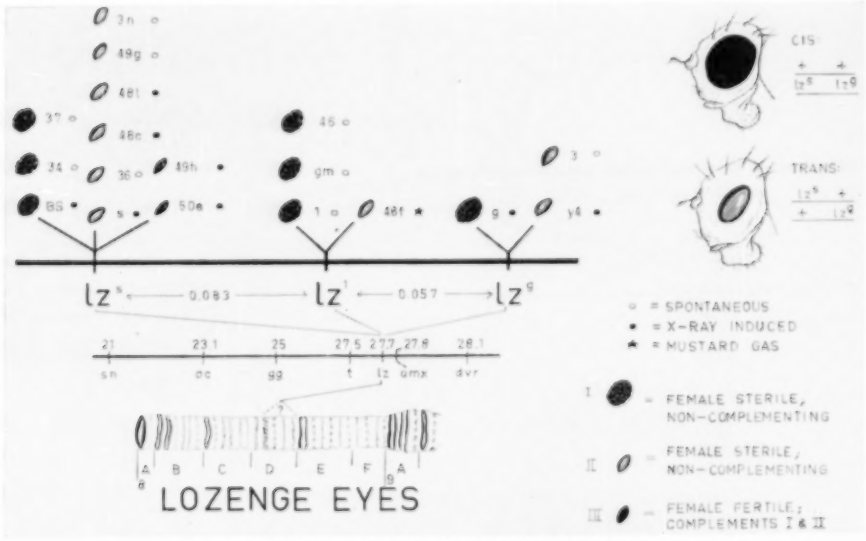

FIG. 4. LOZENGE EYES IN *Drosophila melanogaster*

lz^{s}, spectacled; *lz*^{1}, lozenge; *lz*^{g}, glossy. Note the presence of all three phenotypes at the spectacle sublocus. *sn*, singed bristles; *oc*, ocelliless; *gg*, goggle eyes; *t*, tan body color; *amx*, almondex eyes; *dvr*, divers wings, bristles, etc.

morphology of tarsal claws. Some eighteen members of this system have been localized to three loci. However, the phenotypes are not correspondingly distributed to these loci since several class I and class II mutants occur at all three loci. Similarly the first locus in this series, *spe*, shows all three classes of phenotypes. One of the most important features of this system has been the repeated failure to obtain recombinations between members of the same sublocus, in spite of relatively large numbers counted altogether in numerous combinations employed in the trans compound. In each of these subloci both x-ray and spontaneous mutants occur.

The heterozygous compounds also demonstrate interesting genic action. Compounds involving two different sterile mutants show fertility greater than that of either homozygous allele, a situation opposite to that usually found for trans compounds of alleles (Oliver and Green, 1944). Such differences between compounds and homozygotes are not found, however, with respect to tarsal claw development (Chovnick and Lefkowitz, 1956; Chovnick, Lefkowitz, and Fox, 1956). In this situation the entire lozenge region acts as a single unit, irrespective of the site altered by mutation, and the effects in the heterozygote show a simple dominance relation on the basis of the known expressions of the homozygotes.

The two mutants of class III phenotype, although very extreme as homozygotes and in combination with one another, are almost complementary or wild type in combination with members of class I or II phenotypes even when the same sublocus is involved for both classes. (A similar case involving complementary lozenge mutants reported by Muller in 1932 may have involved the same process). These different investigations of the pleiotropic interactions in the lozenge region illustrate that complexity among compounds cannot necessarily be predicted simply on the basis of the homozygous phenotypes alone, merely because one of these pleiotropic characters does show predictability from the quantitative or qualitative relations of the homozygotes. Indeed, typical pseudoallelic cis-trans differences which are observed on a visible level are not detectable on the antigenic level, report Fox and Chovnick (1954). Deficiencies for the lozenge region permit any of the three phenotypic classes to be expressed in the compound, including the class III mutants, which, it should be remembered, are ordinarily complementary with the other two classes.

Vermilion Eyes (X, 33.0)

(Fig. 5)

At first, vermilion and its alleles seemed to present a spatial as well as functional discontinuity (Green, 1954). Two types of vermilion alleles were known; those which could be suppressed by suppressor of vermilion (su^2-s) and those which could not. Furthermore, suppressible mutants could produce the brown pigment for a wild-type eye if starved in the larval stage; unsuppressible mutants could not. Both types respond to supplied formylkynurenine or kynurenine; both types accumulate non-protein tryptophan. Most interesting seemed to be the absence of suppressible mutants from x-ray treatments, even though a fair sample of 15 unsuppressed mutants was obtained.

The striking difference between these two types of mutants stimulated Green to test for a spatial separability of suppressible and unsuppressible mutants. The pseudoalleles v^1 and v^{26f} (suppressible and unsuppressible, respectively) were found to recombine with one another. The frequency of recombination was very low and an intensive investigation of this series was not pursued. However, another unsuppressed mutant, v^{6sa}, of x-ray origin, was shown by Fox to be to the left of v^{26f}; neither Barish and Fox (1956) nor Green (1954) were able to obtain recombinations between v^{6sa} and v^1. Hence the functional separation on the basis of suppressibility does not hold for these mutants on a two-locus interpretation. Larval starvation also indicates that v^{6sa} and v^{26f} are functionally similar. The double mutant, v^1v^{26f} is unsuppressed. Immunologically, Barish and Fox (1956) report no detectible cis-trans difference. All of the vermilion alleles contain a certain antigen, V-1; another antigen, V-2, is found in all except v^1; a third antigen, V-3, is found in v^{6sa} and in the double mutant v^1v^{26f}.

Forked Bristles (X, 56.7)

(Fig. 6)

Two loci are known for the forked region. As in the vermilion series, it appeared at first that the region was also divisible into two functionally separate units: a locus which did not respond to suppressor of forked (su-f), and a locus

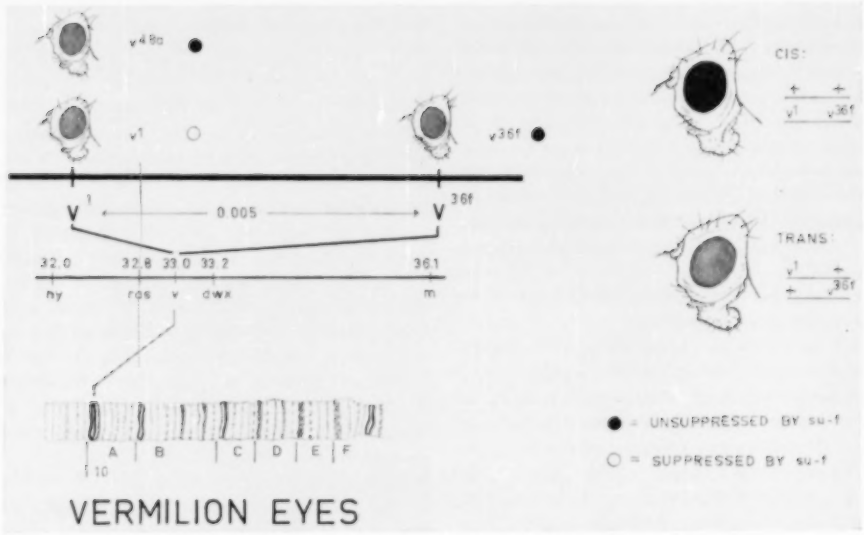

FIG. 5. VERMILION EYE COLOR IN *Drosophila melanogaster*

Note presence of both suppressible and non-suppressible alleles at the v^1 sublocus. *v*, vermilion eye color. Marker genes: *ny*, notchy wings; *ras*, raspberry eye color; *dwx*, dwarfex body; *m*, miniature wings.

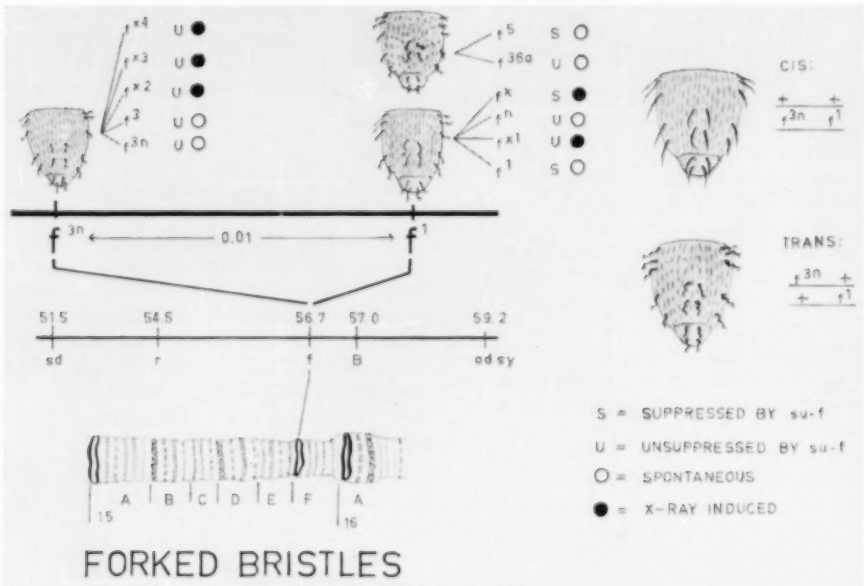

FIG. 6. FORKED BRISTLES IN *Drosophila melanogaster*

f, forked bristles. Note presence of suppressible and non-suppressible mutants at the *f* sublocus. Marker genes: *sd*, scalloped wings; *r*, rudimentary wings; *B*, Bar eyes; *ed*, outstretched wings; *sy*, small eye.

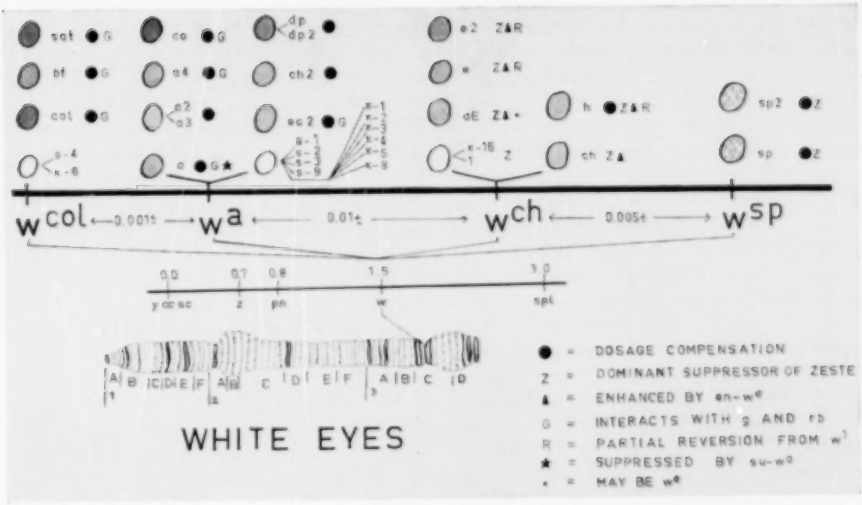

FIG. 7. WHITE EYE COLOR IN *Drosophila melanogaster*

w^{col}, colored; w^{a}, apricot; w^{ch}, cherry; w^{sp}, spotted. s and x, spontaneous or induced white-eyed phenotype. Note the dosage compensation of *li* (honey) in the otherwise non-compensating cherry sublocus. Marker genes: y, yellow body color; *ac*, achaete bristles; *sc*, scute bristles; *z*, zeste; *pn*, prune eye color; *spl*, split bristles.

which did. The separability of these two functional groups appeared even more dramatically than for vermilion, since f^{3} and f^{m}, both unsuppressed, were to the left of the suppressible mutants, f^{1} and f^{5} (Green, 1955b).

Investigations of the x-ray-induced forked mutants seemed to indicate that they were all unsuppressed and allelic to f^{3}. However, one x-ray-induced forked which was suppressible was also found to be allelic to the f^{5} locus (Green, 1957). Furthermore, an x-ray-induced non-suppressed mutant was found to be allelic with f^{1} (Oster, 1958). Thus both loci have been shown to contain x-ray and spontaneous mutants; and both loci show suppressible and unsuppressible mutants. The intensity of the bristle and microchaete disturbance seems to be independent of suppressibility or mode of origin. A salivary doublet is also reported for this region. Total deficiencies for this region are unsuppressible and extreme, as are double mutants such as f^{m} f^{1}, combining suppressible and unsuppressible pseudoalleles of moderate bristle deformity.

The mutant f^{x}, although capable of recombining with f^{3}, is probably a deficiency or rearrangement, since it is non-reverting and arose at the same time as a dominant suppressor of forked (a genetic insertion?) occurred in the proximal heterochromatin of the X chromosome. Reverse mutations have, however, been obtained at both subloci, both spontaneously and with the use of x-rays. Attempts to obtain further subloci by recombination involving members of the same sublocus have not been successful.

White Eyes (X, 1.5)

(Fig. 7)

White eyes was the first multiple allelic series known in *Drosophila*. It has intrigued investigators because of the large number of shades which are present in this series, ranging from white to nearly red. In addition, some of these mutants do not show the same phenotype in the male as they do in the female (where the eye color will be somewhat darker). Such mutants, like eosin, played an important role in the study of dosage compensation, i.e., the capacity of a single dose of a gene in the male's chromosome to exhibit the same intensity of expression as two such doses in the female (where, of course, two X chromosomes would be present).

With the discovery by Lewis, in 1952, that white and apricot are separable by recombination (a discovery made independently by Mac-

Kendrick and Pontecorvo in the same year) the white-eyed series became another instance of pseudoalleles. In the most thorough analysis of this region to date, two different interpretations have been offered. Green (pers. commun.), from a study of more than 30 alleles, has shown that the white phenotype is present at three subloci within this region. However, in terms of function there seems to be a corresponding spatial separation for the dosage-compensating alleles and for those which can suppress a nearby gene, zeste. MacKendrick and Pontecorvo (see Pontecorvo, 1958) using 12 or more alleles, have independently demonstrated spatial and functional separation with respect to zeste-suppressing alleles but not with respect to dosage compensation. The significant differences in the interpretations of these complex loci will be considered later.

There are undoubtedly three loci, but claims for the existence of a fourth have been made for at least three other members of this series. The first, w^{aE}, apricot of Edinburgh, was not followed up and not formally presented. (See reference in Pontecorvo and Roper, 1956). Its status is controversial. The second suggestion for a fourth locus—white-spotted (w^{sp})—is anomalous in showing a variegation without evidence of a visible rearrangement; its status is also ambiguous since the alternative of a minute insertion or rearrangement exerting a position effect on the white locus cannot be easily dismissed (Lewis, 1956). The finding of a second allele of white-spotted (w^{sp2}) suggests that it may really occupy a specific site in the region (Green, 1958). The third suggested member for this locus, w^{Bwx}, Brownex, unlike the other members of the white series, shows a heterozygous dominance resulting in a darker eye shade (actually, flies heterozygous for $w^1/+$ also show a slightly darker eye shade, Muller, 1935b). As a homozygote the eye color is brown. Unlike the two other suggestions for a fourth locus, w^{Bwx} is considered to be to the left of the known loci, rather than to their right (Judd, 1958).

There is also an unsettled question concerning the status of eosin and apricot. Eosin, it is worth noting, arose from white by a partial reverse mutation. Hence it would be expected to retain its allelism if suppressors at other loci were not involved in its causation. Thus the report that eosin (Edinburgh) is to the left of white; and that apricot (Edinburgh) is allelic to white, seemed the reverse of the situation found by Lewis. Apparently the confusion can be resolved if w^{eE} is considered to be apricot, and if w^{aE} is considered to be eosin, the two cultures having had their labels accidentally switched in past handling or in transit (Lewis, 1958). In MacKendrick's analysis, however, w^{aE} consists of two subloci, w' and w'', with w' expressing a white phenotype and w'' of unknown phenotype but acting as a partial suppressor of w'. Thus w^{aE} would be $w'w''$. Green has not reported evidence for such a multiple structure of eosin.

Further complications have been reported by Judd (1958) and by Green (1958b) for the crossover products of some of these pigmented pseudoalleles. The supposed double mutant recombinants in some cases are white but can carry the outside markers in either direction. Analysis of such a case by Green indicates this to be another region where unequal crossing over and non-homologous pairing are apparently under genic control. The deficiencies thus produced give the exceptional white phenotype.

Singed Bristles (X, 21.0)

(Fig. 8)

Pseudoallelism was suggested in this series by preliminary analysis of Ives and Noyes (1951), who reported sn^3 to be to the left of sn^{2wk}. A more exhaustive analysis by Hexter (1957) has revealed three loci. But on the basis of a phenotypic classification Bender and King (1958) suggest four categories: Class I, sterile, kinked hairs and gnarled bristles, and ovaries with stage 14 abnormalities; Class II, fertile, normal hairs and kinked bristles; Class III, fertile, kinked hairs and gnarled bristles; Class IV, sterile, normal hairs and gnarled bristles, and stage 12 ovarian abnormalities. Precise separation of these classes into corresponding loci does not seem to be established since sn^{2wk} and sn^3, which belong to separate phenotypic classes, have not yet been separated. Certain double mutants, combining fertile members such as sn^3 sn^2, are semisterile (Hexter, 1958c). Other peculiarities in bristles can be obtained from various compounds involving these pseudoalleles and their double mutants. Several other existing alleles are available for analysis, and further work on this locus should be rewarding.

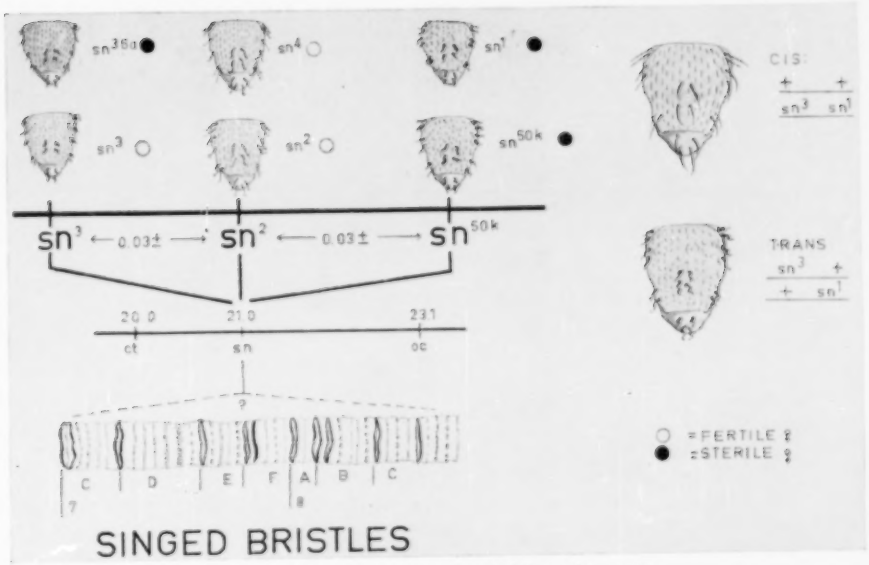

FIG. 8. SINGED BRISTLES IN *Drosophila melanogaster*
sn, singed. Males of singed genotype are fertile. Marker genes: *ct*, cut wings; *oc*, ocelliless.

Garnet Eyes (X, 44.4)

(Fig. 9)

One of the most controversial series of pseudoalleles involves garnet eye color. The major difficulty here seems to be the detection of double mutants. In Chovnick's analysis (1958a) three loci have been reported, on the basis of the combination of markers to left and right in recovered wild types in attached X and free X heterozygous females. The garnets used by Chovnick involved similar phenotypes, although the apparent double mutant ($g^{2oc}g^{a}$) is somewhat darker than the lighter more orange (g^{2oc}) member and is distinct from that of the brown (g^{a}) member. Hexter (1958a, b) however, used a pair of *garnets* in which one of the members (g^{55ad}) was distinctly lighter. In several attempts to obtain crossovers, Hexter recovered wild types but no distinct double mutant on the basis of a phenotypic examination which assumed that a much lighter type would occur if the situation were analogous to that at the white locus, where the double mutant is usually lighter. Experience with the Star and Stubble mutations, however, indicates that the more extreme member need not necessarily predominate in determining the expression of the double mutant. No orange g^{55ad} males were recovered in attempts to extract them from the supposed double mutants. The difficulty in both investigations relating to this series is the extreme rarity of recombination (or wild-type reversions) in this region. It is the tightest allelic series yet analyzed. Both authors have thus claimed that certain wild types, which are not associated with recombination of outside markers, can be interpreted as "conversions" or aberrant crossover events. Hexter does not yet consider the garnet region as a proven pseudoallelic series.

Chovnick's later investigation (1958b) employed another method for the detection of the double mutant—spectrophotometric analysis of the pigments in the suspected doubles and in the component alleles. This approach has been successful in showing an unambiguous difference between expected doubles and single mutants. Whether reverse mutations or more complex genetic mechanisms are responsible for the exceptional wild types in Chovnick's and Hexter's experiments is still unsettled. It is interesting that in both situations the "conversion" phenomena are associated so far with only one of

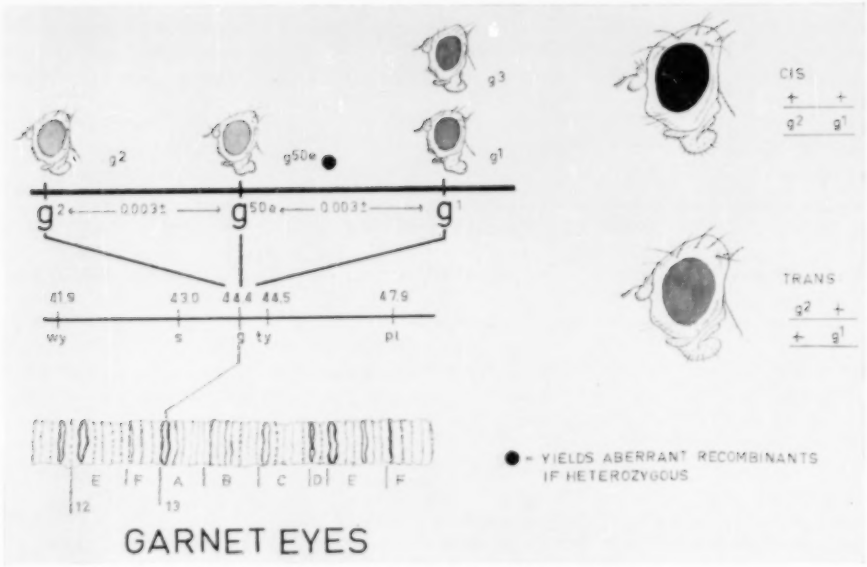

FIG. 9. GARNET EYE COLOR IN *Drosophila melanogaster*
g, garnet eye color. Marker genes: *wy*, wavy wings; *s*, sable body color; *ty*, tiny body size; *pl*, pleated wings.

the alleles used (g^{52d} in Hexter's and g^{50a} in Chovnick's).

Bithorax (III, 58.8)

(Fig. 10)

The bithorax series is of special importance in the evolution of wings and halteres in insects (Lewis, 1951, 1954b, 1957). As a homeotic mutant of excellent penetrance, the series affords a wide variety of qualitatively and quantitatively varying alleles. It also presents some interesting problems regarding the interpretation of complementation or the tendency for the wild-type appearance in a trans compound. The major difficulty to the comprehension of an otherwise clear analysis is terminology. It might be useful, therefore, to summarize the effects of these mutants in development and in their proper map order. (*bx*) bithorax: a recessive which transforms the anterior metathorax into an anterior mesothoracic structure resulting in a partial conversion of the haltere into a structure resembling the anterior portion of the wing. (*Cbx*) Contrabithorax: a dominant homozygous-viable mutation resulting in a conversion of the posterior mesothorax into a posterior metathoracic structure, giving the appearance of a wing mutation in which the normal wing is reduced in size and shape, the posterior portion resembling a haltere-like protuberance. (*Ubx*) Ultrabithorax: a dominant, homozygous lethal, which transforms the anterior metathorax into an anterior mesothoracic form, resulting in an enlargement of the haltere when in trans configuration combined with the wild type. In compound with other mutants of this series an exaggeration of the effects can be observed. Deficiencies of the region are similar to *Ubx* in phenotype and behavior. (*bxd*) bithoraxoid: in this recessive two functions are involved—conversion of the posterior metathorax into a posterior mesothorax, and transformation of the first abdominal segment into an anterior metathoracic segment resulting in a drastically abnormal fourth pair of legs (on the converted first abdominal segment) and transformation of the haltere into a posterior wing structure. (*pbx*) postbithorax: the terminal recessive which transforms the posterior metathorax into a posterior mesothorax, with consequent conversion of the haltere into a vestige resembling the posterior portion of the

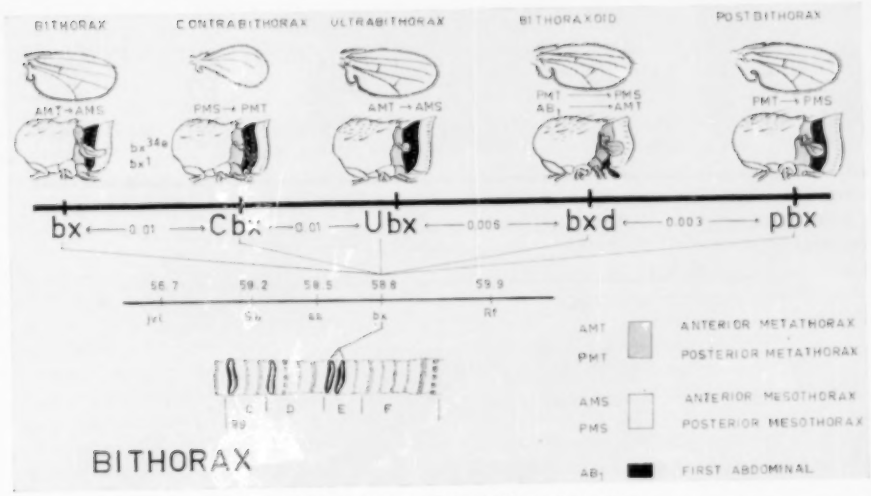

FIG. 10. BITHORAX IN *Drosophila melanogaster*

Note the manifold effects of each sublocus wing, haltere, thorax, legs or abdomen. Note especially the alteration in wing by *Cbx* and the fourth pair of legs in *bxd*. Marker genes: *jvl*, javelin-like bristles; *Sb*, Stubble bristles; *ss*, spineless bristles; *Rf*, Roof wings.

wing. It should be emphasized that this series controls the conversions of the thoracic regions, and not merely of the haltere, although the most striking effect is seen in the homeotic expressions of the haltere.

From these functional aspects, Lewis was able to predict and synthesize a fly with two pairs of wings (and two thoracic scutellums in tandem) by combining *bx* (which causes the haltere to form an anterior wing portion) and *pbx* (which makes the posterior portion of the wing from the haltere). The resulting pair of wings is strikingly normal in appearance in most instances and evokes a very stimulating interpretation of the evolution of insect structures.

The studies of the bithorax series led to an interesting discovery of the relations of these mutants with one another in trans compounds. Lewis (1954) noticed that in the form bx^{34e}/Ubx a relatively stable mutant phenotype could be described. If, however, either bx^{34e} or *Ubx* was inserted into rearrangements (*R*) involving the *same arm* of the third chromosome, then the forms $R(bx^{34e})/Ubx$ or $bx^{34e}/R(Ubx)$ would be more extreme in their mutant expression. Using this principle, called the *transvection effect*, Lewis was able to detect a large number of induced rearrangements in this arm of the third chromosome. Apparently the majority of breaks, encompassing a chromosome region of 500 salivary bands from the *bx* region, are capable of altering the expression of the trans compound. This was interpreted by Lewis as an indication of interchromosomal diffusion of the products derived from these *bithorax* alleles from one homologue to the other. That this is not necessarily a phenomenon characteristic of all trans combinations is demonstrated by the difficulty in obtaining an unequivocal transvection effect in the compound *bx/bxd* (Lewis, 1958). How universal this phenomenon is and exactly what mechanism lies behind it are still unsettled problems.

Dumpy (*II, 13.0*)

(Fig. 11)

Another series affecting qualitatively different traits is the dumpy series (Carlson, 1957, 1958a,b,c). It is of historical interest as the first multiple allelic series showing such qualitatively differing traits (Muller, 1919). The three major effects are all recessive and result in oblique wings (*o*), thoracic vortices and bristle disturbances (*v*), and lethality (*l*), which takes place at some stage prior to pupation. All possible combinations of the *o*, *l*, and *v* effects have been

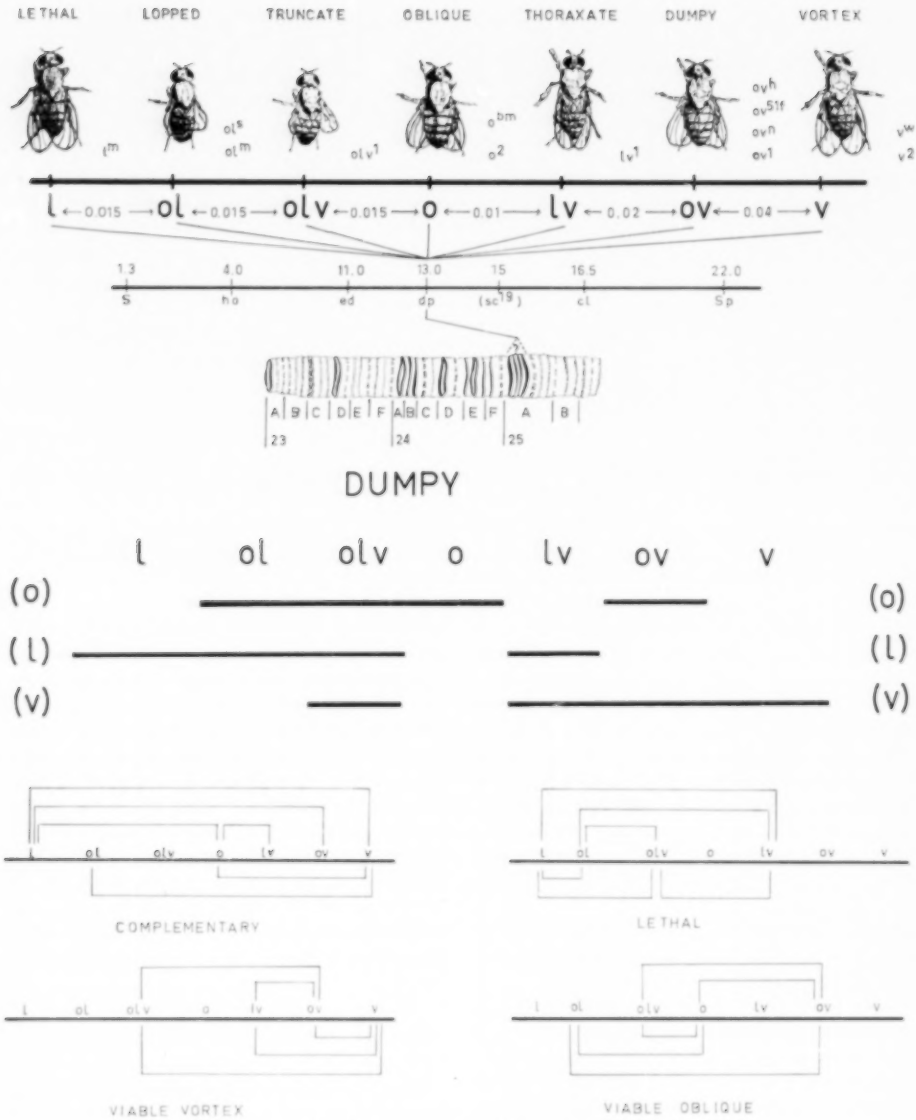

FIG. 11. DUMPY IN *Drosophila melanogaster*

o, oblique wing effect; *l*, lethal effect; *v*, vortex effect. Note that each sublocus has its own combinations of these effect. In the lower figure, note the discontinuity in the *o*, *l*, and *v* expressions along the linear gene map. The various phenotypic expressions in the trans compounds may be determined by consulting the four maps at the bottom. Of especial interest are the numerous complementary trans compounds which do not show a relation to the distance of the sites within the map of the dumpy region. Marker genes: *S*, Star eyes; *ho*, held-out wings; *ed*, echinoid eyes; sc^{19}, break point in the scute-19 translocation; *cl*, clot eye color; *Sp*, Sternopleural bristles.

found as independently arising mutations, resulting in a set of seven phenotypically distinct mutants and one wild type. Recombination analysis reveals the following map sequence: *'l 'ol 'olv 'o 'lv 'ov 'v*, where the first four members are tentatively localized on the basis of recombination rate differences with the standard reference *'ov*. The last four members are directly determined. [The apostrophe (*'*) is used to designate a sublocus whose pleiotropic effects are listed after it.] In general only those effects are expressed which are shared by two trans members in common. The remaining effects are complementary. Thus the central pair, *'o²/'lv* is complementary or wild type in appearance. It is located within the pair *'olv/'ov*, which shows an extreme mutant (*ov*) expression. In turn, this pair is within the pair *'ol¹/'v²*, which is again complementary or wild type. Neither the *o*, *l*, nor *v* effects show continuity in map sequence. For this reason it is impossible to construct a linear complementation map which would correspond to the order obtained by recombination analysis (Carlson, 1958b). No direct evidence has been obtained yet for a "transvection" effect. Double mutant combinations exhibit varying degrees of intensification of the *o*, *l*, and *v* effects. The double mutant *'o² 'v²*, which is viable in the homozygote, is lethal with *'lv*, *'olv*, and double mutants involving these members. It is semilethal with *'ol¹*, *'ol⁺ 'v²*, and *'l*. It is viable with *'ov¹*, *'o²*, *and 'v²*. Pseudoallelic lethality is suggested by the discontinuity in the *l* effect (Carlson, 1957). Attempts to obtain evidence of further loci by recombination of members of the same sublocus such as *'ov*, have been unsuccessful. Variegated position effects can be induced in this region, as is possible also for white, forked, Notch, and asteroid. Deficiencies for the dumpy region show the extreme *olv* expression. Developmentally the traits are expressed at different times: the lethal somewhere prior to the beginning of pupation (and probably embryonic); the oblique wings at the 13th-14th hour after pupation commences, and the vortices between the 6th-10th hours of pupation (Blanc and Child, 1937).

Notch (*X*, *3.0*)

(Fig. 12)

Notch is similar to the dumpy series in respect to several features—the effects occur in qualitatively different characters and show complementation for their recessive features when not in

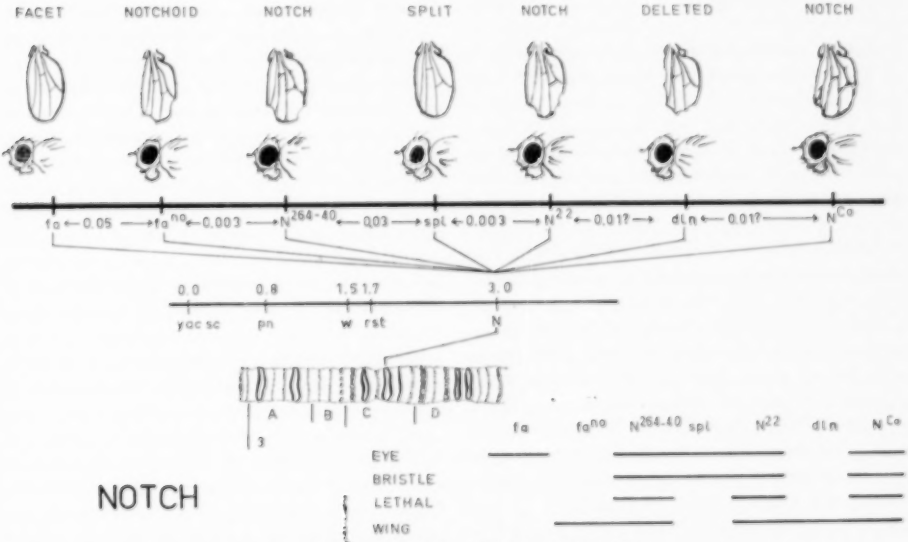

FIG. 12. NOTCH IN *Drosophila melanogaster*

Note the discontinuities in each of the pleiotropic effects with respect to linear distance of the gene map. Marker genes: y, yellow body color; *ac*, achaete bristles; *sc*, scute bristles; *pn*, prune eye color; *w*, white eye color; *rst*, roughest eyes.

common (Glass, 1933; Welshons, 1958a,b,c). The recessive elements involve a notching of the wings (*fa*^{n}, *fa*$^{n\,o}$, *dln*); roughening of the eye facets (*fa*); and splitting of the bristles (*spl*). In addition a dominance for the wing notching is present in a series of mutants involving deficiencies, position effects, and point mutations in this region (*N*). The order of these mutants, as worked out by Welshons, is as follows: *fa fa*$^{n\,o}$ *N*$^{264-40}$ *spl N*^{322} *dln N*^{Co}. The pseudoallelism of the lethality of Notch mutants in the sequence above is critically demonstrated in this series (Welshons, 1958b). Note that these point mutation Notch mutants in trans compounds permit the expression of mutants with bristle, eye, and wing abnormalities or recessive lethal effects. Also note that, like dumpy, none of the recessive effects is continuous in the map sequence. One complication encountered in this series which has not been met with in dumpy is apparent aberrant recombination (conversion or unequal crossing over). A complete analysis of these exceptions should prove to be exciting.

IS PSEUDOALLELISM A UNIVERSAL PROPERTY OF MULTIPLE ALLELES?

As a consequence of the interest aroused by the discovery of pseudoallelism and its implications for gene structure and action, investigations were made to see not only how frequently it occurred in *Drosophila* multiple alleles but in those of other organisms. Among the higher organisms, phenomena similar to pseudoallelism were reported by McClintock and other investigators in maize. In an apparently allelic series of green (normal), yellow green, pale yellow, and white seedlings, McClintock (1944) reported that the yellow green and pale yellow mutants, both of which could be expressed in compound with white, were complementary or wild type with each other. Cytologically, these three mutants revealed the following information—white was a deficiency which involved two loci, pale yellow and yellow green. Pale yellow was also a deficiency but only for its own locus and not for that of yellow green. Yellow green was an apparent point mutation without visible rearrangement. Hence the trans compound of yellow green/pale yellow might be rewritten *py*$^{+}$ *yg*/*Df*(*py*$^{+}$) *yg*$^{+}$. The two adjacent loci were capable of independent function and hence gave the complementary expression in the trans configuration. Either mutant could, of course, be expressed in compound with the total deficiency, white. This system is more analogous to that of achaete and scute (Muller, 1935) or miniature and dusky (Slatis and Willermet, 1954) in Drosophila—being so-called "semi-allelic" genes which do not show a mutant expression in trans, although adjacent and similar in phenotype (see review, Komai, 1950). That such a classification is somewhat arbitrary, however, can be demonstrated in the Notch and dumpy series mentioned before, in which both semi-allelic and pseudoallelic expressions can occur.

The studies of Laughnan (1955) illustrate a high degree of complexity in expressions for the *A* series of mutants in maize. The *A* series affects the anthocyanin pigments present in the endosperm aleurone. Other effects of these mutants change the pattern of colors in pericarp and in the vegetative tissues. Heterozygotes for two of these mutants, A^{b}/a, gave two types of exceptional progeny—stable mutants of a pale phenotype (A^{d}-*s*) and unstable mutants of the same phenotype (A^{d}-*m*). Another compound involving the A^{b} mutant, A^{b}/a^{b}, also gave the stable A^{d}-*s* exception, but instead of a mutable A^{d}-*m* it gave a stable A^{r}-*s*, showing a faint coloration. Laughnan's analysis indicated a duplicate structure of the A^{b} mutant, the components of which he designated α and β. The A^{d}-*s* type was found to be the α component alone which was crossed out of its association with β. This made the A^{d}-*m* type another duplicate structure: αa. The faint allele, A^{r}-*s*, was stable, although duplicate αa^{b}, because the *a* allele determines the mutability of the phenotype, as suggested by its response to the specific mutator gene *Dt*, Dotted. Laughnan was thus able to predict that homozygous A^{b}, being compound, should also give off the stable A^{d}-*s* (α) exceptions if there were synaptic equivalence between the two components, as in the case of the duplicate regions of the Bar mutant. This was borne out by the appropriate tests.

A similar situation was found for the *R* series studied by Stadler and his colleagues (1953, 1956). Unequal crossing over arising from a synaptic equivalence in this region has resulted in a series of alleles which show distinct disturbances in color pattern in the seed and plant tissues. Cytologically these exceptions are apparently unchanged. Since these mutants can be complicated sequences of duplicated and missing segments in this region, Stadler rejected the terms "deficient" and "duplicate" as being too misleading since

the ancestral form was not known and viability was apparently unaffected by these unequal crossover products. It was this high degree of complexity arising from unequal crossing over between genes which led him (1954) to seek an operational definition of the gene that would avoid the difficulties of hypothetical models within which all the complicated data would have to be squeezed. However, this definition of the gene "as the smallest segment of the gene-string that can be shown to be consistently associated with the occurrence of a specific genetic effect" (Stadler, 1954), is not helpful, operationally, for regions like Notch and dumpy were the effects expressed are qualitatively distinct. In Goldschmidt's investigations it would be the chromosome itself, for the step-allele theory it would be the subgene, and, as will be pointed out later, this can even lead to a "gene" of only a few nucleotides in length.

Thus the work in maize genetics indicates a considerable degree of gene complexity which is associated with unequal crossing over, very similar to the Bar case, but involving much smaller regions of genetic material, and apparently capable of position effects for the changing phenotypes observed in these exceptional recombinants.

A possible case of true pseudoallelism in maize may exist at the Waxy locus. Nelson (1958), using an ingenious technique of staining pollen grains with iodine, has been able to obtain wild types (black coloration or starch-producing) from various pairs of Waxy alleles (red coloration, non-starch-producing). The rate of occurrence for these recovered black pollen grains is much higher than those found in homozygous Waxy pollen grains. However, a linkage test cannot be performed yet by this technique, and without this essential test the complexity at this locus remains uncertainly one of a normal pseudoallelic region.

In other plant material, such as cotton, there is a possibility of duplicated genes with divergences in function, as revealed in interspecific crosses carrying members of similar allelic series (review, Stephens, 1952). Although such amphidiploid hybrids may act hemizygously for certain of these alleles, it is not critically established that the mechanism involves divergent duplicated loci unless the allelic region itself is incorporated into either of the parental species' genome. A system similar to the Rh and dumpy series is reported for the anthocyanin (R_z) series in Asiatic cotton (Stephens, 1948). Originally three adjacent loci were suggested, *G*, *S*, and *M*—with *G* and *S* together capable of forming the anthocyanin petal spot. *M* was presumed to regulate anthocyanin distribution along the petal margins (Yu and Chang, 1948). Attempts to correlate these three genes with the known biochemical processes found to occur in the anthocyanin synthesis for these petals were not borne out experimentally. Whether the assumption of a three-locus system is justified, therefore, cannot be assured without a thorough recombinational analysis of the multiple alleles involved in the R_z system.

In other animal species there are several allelic series which provide a good deal of interest for developmental studies and gene action. Of particular interest is the series of known linked genes affecting tail development in mice (the *t*-series). The mutants Brachy, Fused, and Kinky recombine with one another. Other members of this series seem to show a variety of differences with regard to recombination and trans interaction of expression. Because of the large numbers required for a recombinational analysis, the precise status of this region is still uncertain (See review, Dunn, 1956). Coat color genes also depend on analogy for their supposed pseudoallelic relations.

A remarkable series of alleles controlling features similar to those of the dumpy and bithorax series is found in the *E* series of *Bombyx mori*, the cultivated silkworm. In this series at least 15 members have been discovered. Among the effects expressed in this series are supernumerary legs, supernumerary lunar patterns on the larva, suppression of certain patterns on the abdominal segments, and lethality. Pleiotropic effects of perhaps a secondary order are found in malformed ganglia and shortened legs in the adult moth. Recombination with typical cis-trans differences has been obtained between E^H and E^K by Tsujita (1955). The region for the *E*-series shows very similar continuities and discontinuities for the various pleiotropic effects that dumpy and Notch exhibit.

Attempts to justify genetic complexity for blood group loci are based on two approaches—an immunological distinction between the antigens produced by a series (review, Race and Sanger, 1954) or a statistical analysis of the frequencies of the blood groups in populations and

how they would be distributed if the region were of a pseudoallelic or linked nature (Fisher, 1946). Objections to both of these methods have been made (Wiener, 1954; Carlson, 1958c). As Stormont (1955) carefully points out, "it is significant to note . . . that all the numerous suggestions and the few explanations which have so far been advanced to the effect that linked genes (or pseudoalleles as used synonymously by certain writers) are involved in the control of blood groups do not trace to any real genetic evidence. Rather, most of them trace both directly and indirectly to the long disproved idea that there is a strict one-to-one correspondence between antigen and antibody. If the basic premise is wrong, it follows that the explanation is likely to be wrong."

Actually the interpretation of blood groups is more complicated than is usually assumed. Superficially, it would seem to yield itself to a test by recombination. However, such recombinations must be unambiguous even if linked markers are available for a critical test (see, for example, the alternative models cited by Glass, 1949, which could be used for either positive or negative recombination results). In the absence of such linked markers, a technique such as Nelson has employed for the Waxy locus in maize might be used. These two methods are not sufficient to demonstrate that the various antigens produced by a blood group, such as the Rh series, are the products of separate subgenes or pseudoalleles which correspond spatially and functionally.

In the Rh series, for instance, we might find one parent with a genotype *CDe/cdE* (R_1/r''), using the former designation for the triply-linked loci of the Fisher-Race interpretation and the latter designation for Wiener's multiple allelic interpretation. The other parent under consideration might be *cde/cde* (r/r). Assuming proper safeguards for the legitimacy of the offspring, a child of the genotype *CDE/cde* (R_z/r) would be, in the Fisher-Race theory, a possible instance of recombination between the *D* and *E* linked loci in the *CDe/cdE* parent. In Wiener's interpretation either R_1 or r'' mutated to R_z. However, if *'CDe* represents the pleiotropic effect of the entire Rh region when altered in a specific region or mutant site, and if *'cdE* represents the pleiotropic expression of the Rh region when altered in a different site along its molecular length, then recombination within the Rh region would result in a double mutant which might be designated *'CDe 'cdE*. Such a double mutant would be almost indistinguishable from the usual *'CDE* found in the general population.

By way of analogy, the dumpy series illustrates a remarkable parallel. The three pleiotropic effects form a series of eight genotypes, just as in the Rh series. If *'olv* represents a point mutation from the wild type to the most extreme member of this series, then the same phenotype can be put together by combining different subloci. Thus *'o 'lv* and *'ol 'v* represent two such recombinant types. In addition, recombination can produce *'lv 'ov*, which again contains the same pleiotropic elements. Similarly, *'l 'o 'v* and *'ol 'ov* can be put together. The important consequence of such synthetic *olv* mutants is their similarity to the point mutation itself and the rarity with which one would expect to find them in nature. Each such *olv* mentioned would represent a region whose alterations occurred in quite distinct places along the molecular length and whose sites could be demonstrated by a recombination test. Furthermore, the dumpy analysis has conclusively ruled out a correspondence of the *o*, *l*, and *v* effects to three separate pseudoalleles whose various combinations would produce the eight genotypes in this series.

These considerations and others (see Carlson, 1958c, and Pontecorvo, 1958) exclude recombination alone as a sufficient demonstration of a "one gene—one antigen" model for blood group series. Moreover, they imply that nomenclatural controversies must be settled by arguments in behalf of priority, convenience, or the resemblances which these blood groups have to complex loci in laboratory organisms.

Thus it is premature to state that pseudoallelism is a universal phenomenon in all organisms, since the degree of recombination analysis possible in the best-known laboratory species has not been duplicated in the higher forms. But it would seem more than peculiar for *all* these laboratory organisms to show some evidence of gene complexity whenever it has been diligently sought for. At best, therefore, we are inclined to give ourselves the benefit of the doubt and accept the view that complex loci are of widespread occurrence in the plant and animal kingdoms, although we should keep in mind that the

proof is not as elegant as we would desire experimentally.

COMPLEX LOCI IN MICROORGANISMS

The initial studies of complex loci in *Drosophila* and other multicellular organisms indicated a need for large counts in any crossover or mutation analysis of single gene regions. Thus the use of microorganisms in genetics has provided a necessary and valuable tool for these approaches to an understanding of gene structure. However, the various microorganisms used seem to show some differences in the type of genetic organization which they possess. This diversity of genetic systems may only be an apparent one because of the short time during which these organisms have been genetically investigated. In the next few years enough information should be available to determine the unique and common features of these organisms. At the present time, however, there is a tendency to generalize the findings from one organism to those of all living material, a process which has led to conflicting interpretations of genetic structure and action. In this section, for convenience, the microorganisms will be considered in an ascending order of complexity rather than in their historical sequence as contributors to the study of complex loci.

Viruses

The analysis of the *rII* region in the *E. coli* T-series bacteriophage has constituted one of the major advances in genetic knowledge (review, Benzer, 1957). In the *rII* region, which is about six map units in length, there are two adjacent regions, each one of which is involved with the production of a larger plaque phenotype (rapid-lysis). These have been designated as *A* and *B*. The *rII* mutants are isolated on *E. coli* strain B, where they form much larger plaques than does the wild type phage. They are assayed on *E. coli* strain K, which does not lyse when infected with individual mutant varieties of *rII*. The wild-type T4 phage does cause infected K cells to burst. Hence, when two independently arising mutants of *A* (or *B*) are incorporated as a mixed infection, the host K bacteria will usually give a small percentage of wild-type recombinants. This test, analogous to the cis-trans test for pseudoallelism, also demonstrates that double mutants (which can be detected by special techniques) are complementary in a mixed infection involving them with the recombinant wild types. However, if mutants from *A* and *B* are introduced together in a mixed infection, their progeny are capable of lysing the K strain. For this reason *A* and *B* are considered functionally different by the cis-trans test. Benzer has defined such a functional unit as a *cistron*. In length, the size of a cistron is determined by the maximum recombination distance between its various members. For *A* it is about four map units; for *B* it is about two map units. The cistron can be considered the gene as a unit of function.

The various *rII* mutants which were obtained (over 900) were tested by these techniques for their map relations. In *A* about 33 sites were detected in a sample of 241 mutants; in *B* about 18 sites were analyzed. By meticulous analysis of all the mutant members covered by a small deletion in one of the cistrons, Benzer was able to estimate that about 100 sites are present in the *A* cistron, and about 50 in the *B* cistron. These individual mutations are capable of recombination with one another in most instances. The minimum recombination frequency between mutations free of detectable rearrangements is about 0.02 map units. Hence this unit of minimum recombination has been called the *recon*. It may be considered to define a gene as a unit of recombination. The various mutants which were capable of reversions by back mutation average about 0.01 to 0.05 map units in length. Such a unit, defining the gene as a unit of mutation, has been called a *muton*.

By an admittedly tenuous series of assumptions involving the structure of deoxyribose nucleic acid (DNA) according to the Watson-Crick theory and the correspondence of a linear linkage map to a linear DNA molecule containing the corresponding loci, Benzer estimated that the recon was about 2 nucleotide pairs in length; the muton about 1 to 5 nucleotide pairs; and the cistron about 100 nucleotide pairs. In effect, the analysis of the *rII* region suggests, for bacteriophage, a continuity of the genetic material to the nucleotide level. The mutational sites are, for the most part, randomly scattered, although there are more susceptible regions ("hot-spots") in which a clustering of mutants can occur, spontaneously as well as induced.

Even those mutants which do not recombine with other mutants of the same site can sometimes be distinguished from one another by their reversion frequencies. Further investigation of bacteriophage cistrons has shown similar properties for the host range (*h*) region of T2 (Streisinger and Franklin, 1956). Certain features of this *h* region resemble those of the tryptophan synthetase mutants in *Neurospora* and will be discussed in that context below.

Bacteria

Studies in *Salmonella typhimurium* by Demerec and his colleagues (1955, 1956) have produced a remarkable correspondence between gene structure and function. The method employed in this analysis is transduction (Zinder and Lederberg, 1952), with about ten to twenty genes carried by the infecting bacteriophage as a separable chromosome fragment capable of partial incorporation into the host's genetic complex. Studies of nutritionally deficient mutants have indicated a tendency for mutants of similar phenotype to be grouped together in an order which corresponds to the steps in the biochemical synthesis of the particular organic compound for which the locus is defined. In the tryptophan region, for example, the genetic sequence *tryD* → *tryC* → *tryB* → *tryA* corresponds to the biochemical sequence:

$$\xrightarrow{A} \text{(anthranilic acid)} \xrightarrow{B} \text{(compound B)}$$

$$\xrightarrow{C} \text{(indole)} \xrightarrow{D} \text{(tryptophan).}$$

For the histidine region, Hartman (1956; and pers. commun.) has described a more complex relation, as follows:

$$\xrightarrow{E} \text{(reaction unknown)} \xrightarrow{F} \text{(compound III)}$$

$$\xrightarrow{AH} \text{(imidazole glycerol-PO}_4\text{ ester)}$$

$$\xrightarrow{C} \text{(L-histidinol-PO}_4\text{ ester)} \xrightarrow{D} \text{L-histidine)}$$

$$\xrightarrow{G} \text{(reaction unknown).}$$

(See Fig. 13).

Although these are the two best examples of such linked sequential gene-controlled reactions, there seems to be a tendency for such associations to occur in *E. coli*, too (Skaar and Davidson, 1956). Moreover, the tryptophan region in *E. coli* also shows a series of four adjacent regions in the same order and performing the same sequential reactions as those found in *Salmonella*. Nevertheless, not enough data are yet available to indicate how many of the phenotypes in nutritionally deficient mutants are linked in biochemical synthesis. Within each region of these adjacent genes there are nonidentical alleles which can recombine with one another or show differences in their mutation rates.

Fungi

As the cases of pseudoallelism increased in *Drosophila*, Pontecorvo (1952), who had independently worked on the white eye series, and his colleagues sought a more refined test for its prevalence in other organisms. By using several randomly selected nutritionally deficient mutants in *Aspergillus*, Roper (1950) was able to obtain a low degree of recombination for several such mutant pairs expressing similar phenotypes. In no case did he fail to obtain recombination. For this reason it seemed unlikely that pseudoallelism was a characteristic of only a few loci in an organism, but that the genetic material, at least in *Aspergillus*, was continuous throughout the chromosomal organization. Hence Pontecorvo (1955) predicted that only on rare occasions would a series of multiple alleles fail to show recombinants for all its members. It should be pointed out that just as the bacteriophage required a mixed infection to simulate the diploid state for the cis-trans test, so the *Aspergillus* mutants, which are haploid, required the establishment of a heterokaryon (carrying two nuclei per cell) in order to provide a suitable analogue to the cis-trans effect. After diploidization of the heterokaryon the recombinant products can be isolated and wild types can be selected on minimal media.

In *Neurospora* several matters are worthy of attention. First, unlike the organization of the genetic material in bacteria, the nutritionally deficient mutants are scattered, for the most part, among different linkage groups instead of exhibiting sequentially organized clusters (review, Beadle, 1945). Secondly, the bulk of mutations, spontaneous and induced, seem to affect only one primary process or function. The significance of these two observations in relation

to the theories of gene structure will be discussed shortly.

Of extreme importance to an understanding of gene function is the work of Yanofsky, Bonner, and others (review, Suskind, 1957) on the tryptophan synthetase (*td*) locus in *Neurospora*. In this series about twenty-five independent alleles have been tested for functional differences. Different suppressors not associated with the same chromosome can restore the normal enzyme formation for some of these mutants. This is analogous to the suppressor tests used for *v* and *f* in *Drosophila* to distinguish otherwise phenotypically similar mutants. With the assumption in mind that mutant genes might produce no enzyme, or perhaps inactive enzymes, Bonner and Yanofsky attempted an immunological analysis of this series. Most of the mutants show a strong reaction with anti-tryptophan-synthetase. The substrate antigen in these mutants, called CRM, has very similar properties to the tryptophan synthetase molecule, and can be distinguished only by slight differences in dialysis.

A second class of alleles, which does not respond to the antigen test, and which does not contain CRM, is also unsuppressed by the various alleles of the suppressor loci. Other criteria which serve to distinguish these mutants are their respective ability to function at different temperatures; their capacity to produce tryptophan synthetase at very low inefficient rates; and their ability to accumulate indole (see review, Suskind, 1957). Although early attempts to obtain recombination between these mutants were unsuccessful, this has apparently been accomplished by Weijer (1958) for some ultraviolet-induced *td* alleles. In *E. coli*, Yanofsky (1958) has reported the interesting fact that tryptophan synthetase mutants similarly form suppressible and unsuppressible mutants. Furthermore, reversions can be of suppressor or back mutation origin. Tests for CRM production show that, unlike the *td* situation in *Neurospora*, the mutants lacking CRM in *E. coli* are capable of restoration to normal function by suppressors. This information, together with the similarity in response to suppressors and temperautre differences for some of the histidine mutants in *Salmonella*, suggests the presence of a common feature of the genetic material in most organisms, since it is found also in many of the *Drosophila* allelic series.

Two other items of importance have emerged from genetic studies with *Neurospora*. The first of these is gene conversion (Lindegren, 1953; St. Lawrence and Bonner, 1957). This phenomenon, which has been used by several investigators in slightly different ways, has been considered to involve a recombinational process in *Neurospora*. The conversions usually involve one of the four products of meiosis, the converted strand being sometimes associated with recombination and sometimes not. The conversions are not simply a back mutation process, since the rarity or absence of these reversions from the alleles when homozygous indicates the need for heterozygosity in conversion phenomena. Many models have been proposed as mechanisms for this phenomenon, but none has yet been sufficiently detailed to be put to an experimental test. Thus the phenomenon has been associated with "negative interference" (multiple crossing over within a small chromosome segment), with "non-reciprocal crossing over," or with "copy choice" models of genetic replication (review, Bonner, 1956; St. Lawrence and Bonner, 1957; Mitchell, 1957). Fortunately the phenomenon is not too frequent in occurrence, and linear mapping is not drastically affected unless small regions are investigated. Whether this phenomenon is present in higher organisms is still debatable, although claims for its occurrence have been made in *Zea* (Coe, 1958; Brink, 1958) and *Drosophila* (Chovnick, 1958a), especially for the mutable loci in these organisms (Demerec, 1928, 1954).

Negative interference might involve a different process from gene conversion (or as St. Lawrence and Bonner have cautiously advised, conversion can cover a multitude of mechanisms). It has been reported in *Aspergillus* by Pritchard (1955) and in phage by Chase & Doermann (see Edgar, 1958). The presumed and sometimes actual recovery of the double mutant type and the otherwise linear nature of these mutational sites in these organisms would rule out one of the characteristics of the gene conversion process—the failure to obtain the double mutant while obtaining the wild type. Again it should be emphasized that without tetrad analysis the two processes are only ambiguously distinct from one another.

Pritchard's analysis of negative interference suggests that chromosomes come into contact only in restricted regions (effective pairing sites). Within such sites multiple recombinations can be obtained. The sites, however, are randomly distributed and thus in organisms like *Drosophila* or any population of progeny from several meiotic cells, the overall effect will not disturb the map relations of genes in chromosomes except for *intra-locus* regions under investigation. These will show more recombination than would be expected in such a small length of a chromosome map. The only difficulty of such multiple exchanges in a region like dumpy or bithorax in *Drosophila* would be the absence of even-number exchanges within the effective pairing site. Such even-numbered exchanges would give apparent "reverse mutations" not associated with recombination of outside markers and *double mutants* not associated with recombination of outside markers. The latter type of *double mutants* has not been observed in these regions.

The second interesting development to come out of the *Neurospora* work has been the contributions of Giles, Case, and others to an interpretation of complementation. In the pantothenic-2 (*pan-2*) region a series of mutants which affect the same biochemical step (conversion of keto-valine to ketopantoic acid) show certain trans configurations which complement each other, giving the wild and not the mutant phenotype. The complementing mutants apparently fall into two functional regions both on the complementing level and by recombination analysis. The two regions, *B3* and *B5*, have their own allelic series within which no complementation occurs and within which recombination may or may not occur (Case and Giles, 1958).

From these initial findings of complementation within allelic regions, several investigators have since reported similar findings in *Neurospora* (Lacy and Bonner, 1958; Woodward, 1958) and other organisms (Hartman, 1958). It is assumed, in general, that the use of a complementation map will correspond to the linkage map. That this is only tentative is indicated by the appearance of multiple effect mutants (non-complementing) which are presumed to be rearrangements, but which surprisingly show back mutations to the wild type (Woodward, 1958).

An extremely interesting example of these complementation results has been worked out by Hartman (1958b). In the histidinol dehydrogenase (*D*) locus in *Salmonella typhimurium*, there are two major regions, *a* and *b*. (fig. 13). In region *a* there are three mutational sites which are non-complementing with one another but which complement five sites in region *b*. These five sites in region *b* are also non-complementing with each other, but complement those in *a*. However, there is one site, not a rearrange-

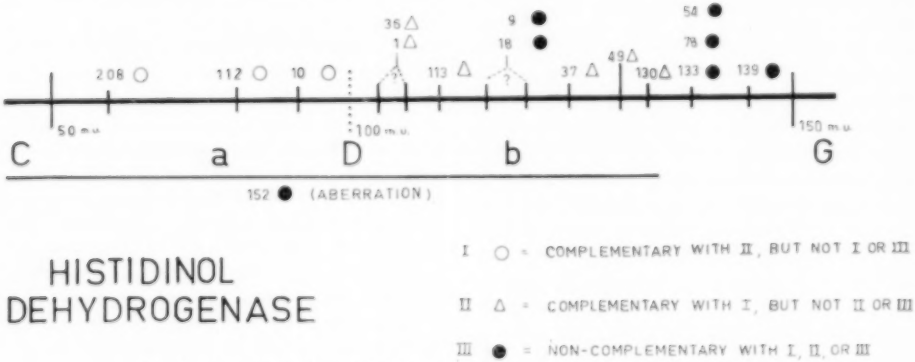

FIG. 13. THE HISTIDINOL DEHYDROGENASE LOCUS IN *Salmonella typhimurium*

C, D, and G represent three of the genes in the linked series responsible for histidine production. Note especially the distribution of the pleiotropic alleles *9* and *18* as well as the four pleiotropic mutants terminating the D cistron. For convenience, D is separated into functional regions *a* and *b* whose members complement each other in a manner indicated in the diagram. The pleiotropic mutants resemble the deficiency *152* in phenotype, but differ by their normal crossing over or recombination.

ment, which lies within region *b* and which does not complement members of either the *a* or *b* regions. There are also two additional non-complementing members which are located to the right of the *b* region. Hence in this system there seems to be a regional grouping of sites. For this reason the precise terminology of the *cistron* employed by Benzer for complementing regions breaks down if we accept the anomalous non-complementing member which, without being a rearrangement, can nevertheless alter the functioning of both regions. This is not unique to the bacterial cistrons or genetic regions. In *Drosophila* several instances of non-correspondence to complementation and linkage maps will be presented in the next section.

In the yeasts, Lindegren (1953) originally reported gene conversion several years prior to the finding of this phenomenon in *Neurospora*. This was recently confirmed by Roman (1956). In later studies of complex loci, Lindegren and Pittman (1958) reported an interesting case which deserves some attention. In the *MZ* (melezitose) locus crossing over has not been observed, but a series of multiple alleles in this region expresses five different characters. Eight of the thirty-two possible types combining these characters have appeared as mutations. Phenotypically, some of these mutants are identical, but their genotypes are different. Indirect mutation studies suggest a single gene interpretation of the series rather than a linked series of five genes. Mutations with multiple effects can show reverse mutation, and accordingly they are not likely to be deficiencies or rearrangements. Certain controversial findings, such as "transformation" by supplied melezitose (without DNA) and "conversion" phenomena as mechanisms for complementation, make it difficult to evaluate the full significance of the genetics of this locus. Although some of these features are very similar to those in the dumpy and Notch regions of Drosophila, it is not valid to make the comparison until more complete data on the *MZ* locus have been published.

This very brief sketch of the genetics of complex loci in microorganisms is only an indication of the vast amount of information being accumulated on this subject in a number of organisms. Reviews of these organisms may be consulted in the papers of Demerec (1956), Hartman (1957), Benzer (1957), and Mitchell (1957).

INTERPRETATIONS OF COMPLEX LOCI

In Lewis's system, each gene is not only a unit of external recombination, but also a unit of mutation and a unit of a single specific function. The pseudoallelic phenomenon is considered to be a position effect *between* genes brought about by the occasional blockage in a sequential transfer of immediate gene products necessary for the formation of a product which cannot be produced efficiently by a single gene. Pleiotropic effects are generally the separate functional activities of the individual loci composing the series. The pseudoallelic loci are believed to be related through a common descent from an original adjacent (but not tandem) duplication, arising, perhaps by a primary unequal crossing over (Lewis, 1951). Complementation, if it occurs in trans compounds, may arise from an *interchromosomal* exchange of immediate gene products aided by somatic pairing, if a "transvection" effect is also present. Where somatic pairing is not involved the complementation may result from immediate gene products which diffuse freely throughout the nucleus (Lewis, 1958). The substances involved in the sequential transfer are somewhat complex, since "each intermediate substance is postulated to act in a dual capacity: as substrate for the succeeding reaction and as a determiner of a specific physiological process." It would appear from this that they are not merely the precursors to a sequence such as that found for the tryptophan and histidine regions in *Salmonella*. They would probably not differ appreciably from gene products of non-pseudoallelic regions as determiners of such specific physiological processes (Lewis, 1955).

A similar theory was put forward by Pontecorvo (1952). In the pseudoallelic regions a clustering of genes regardless of the mode of origination was believed to have been selected for the efficiency in cooperating in the synthesis of chemical reactions involving such labile, minute, and otherwise sensitive compounds that only their close juxtaposition could bring about completion. These reactions were designated as "millimicromolar reactions."

After discovering the prevalence of pseudoallelism in randomly selected regions of *Aspergillus*, Pontecorvo abandoned the conception of separate genes in pseudoallelic regions. Using

instead a physiological model adopted from Goldschmidt's concept of the continuity of the genetic material, Pontecorvo (1955) suggested that these regions should be able to yield far larger numbers of loci than had been detected so far. The mutational sites within such a physiological region would be at least equivalent to the value obtained by dividing the map distance of the entire region by its smallest recombinational distance (Pontecorvo and Roper, 1956). Since mutational events could occur throughout a continuous region, any two mutations of independent origin would not be expected to be altered at an identical site. The cis-trans difference could be accounted for in such a model without recourse to a sequential transfer of products or a need for a special position effect. The difference would be merely an apparent one arising from *intragenic* recombination. The recombinant passing through two mutant sites would always reconstitute the intact physiological region. However, to interpret complementation phenomena in a continuous gene strand, Pontecorvo (1955) suggested that the region, acting as a physiological process, would show a certain optimum value within it, but that the farther away two sites were from this peak value the more they would tend to complement one another. Thus "allelism . . . is a relation between elements of the genetic material which is approached asymptotically as we consider elements located nearer and nearer along the chromosome, or more and more similar in phenotypic effects. To approach this asymptote is the best that we can do at present because we have no basis for predicting from first principles where the actual ultimate functional or structural unit of resolution will lie." (Pontecorvo, 1956).

There is a good deal of similarity between the cistrons found by Benzer in phage and the physiological gene postulated by Pontecorvo. Both show internal continuity by recombinational tests. Both show numerous sites, which can be empirically determined in the case of the *rII* region and which correspond nicely with the values obtained by the division process mentioned. In the cistrons, however, functional distinctness is precise and the regions involved are either adjacent or are not located in the same regions of the gene-strand. In Pontecorvo's model there is a possibility for these physiological regions to be more flexible. "It seems quite possible that at least in some cases the transition between the sites of one system of integration, that is, one gene, and the next may be gradual and with overlaps. . . ." (Pontecorvo, 1956).

Thus both Lewis's and Pontecorvo's theories, postulated for organisms with essentially chromosomal levels of genetic structure, find partial counterparts in the studies of microorganisms. The sequential transfers of Lewis's theory are found in *Salmonella*, although within each gene of the series there are numerous non-identical alleles which can recombine, to give a series of non-overlapping but continuous regions. In Pontecorvo's model continuity is likewise obtained, but the complementation within genetic regions in higher organisms makes the linear distance relation between mutational sites an unlikely mechanism (Carlson, 1958a, b). Thus in the lozenge series there are three loci; yet in one of these there are complementing type III mutants which can give complementation with the type I and type II mutants at any of the three loci. In effect these show the existence of truly complementary alleles. In the dumpy region not only is there the paradox of finding complementary trans combinations of mutants of different phenotype, separable by recombination, but also separable by an interval within which other mutational sites are present. Hence no relation at all is found for distance between any of the three phenotypic expressions or for mutant and non-mutant expression. The same is obviously true for Notch, since the wing, bristle, eye, and lethal effects are discontinuous within the same map distance.

Careful analysis of the dumpy and Notch regions is extremely valuable in pointing out the limitations of the cistron terminology in *Drosophila* pseudoallelic series. If we use it in the vague sense, like the word gene, it is acceptable. If we use it as a very precisely defined operation it has serious weaknesses, conceptually, for an understanding of the behavior of the gene in cellular levels of organization. The gene seems to show patterns even in its discontinuities. In the dumpy region there is a definite tendency for these effects to run together in *three* and *one* distributions. This may be a coincidence, but it could mean that certain regions of a gene are more essential than others to the formation of the gene product or to the type of information it can convey to that product. It also implies that

the sequence in the DNA chain may not always be significant at each nucleotide level—that some may be altered without impairing a particular gene function, by our usual standards of seeking out mutant effects. It leads to a very speculative series of interpretations about spatial requirements for the formation of a gene product rather than mere amino acid sequence from the "coding" of the gene. How, for example, will the structural organizations of the products be affected by mutation?

We need certain basic information before our speculations can have meaning. First, we must know what pleiotropism implies in higher organisms. Is it merely a syndrome effect of secondary and tertiary consequences from one single aberrant gene product? Can a gene with a specific code produce more than one product if its surrounding environment changes, as it certainly does in development? In dumpy and Notch, where these pleiotropic effects are qualitatively different, we have a tool which may someday give us the answers to the problem of pleiotropism. If we assume a single gene product it implies that this product acts differently at different stages of development when the various functions of the gene are expressed. The work done on the dumpy locus provides one clue about pleiotropism for this gene. The expression of the thorax effect is earlier than the expression of the wing effect. The lethality is expressed before either of these effects. Hence, if we consider a gene like oblique (dp^o) we know that this mutant gene is not visibly or functionally abnormal at the time the lethal factor is expressed or at the time the thorax is formed. Hence the dumpy region, although altered, would not be manifestly altered if we did not have the wing effect for its detection! How many slight effects of this type occur, where we have alterations in genes which produce no operationally distinct mutant expressions, is a totally unexplored problem. Its consequence for testing the effectiveness of various mutagens is subtle but important: what percentage of alterations in a gene result in mutant expression? Information on this problem may settle one of the chief controversies in distinguishing genetic structure in *Drosophila* and in microorganisms. Are subgenes in *Drosophila* really distinct units of recombination, or are they mere "hot spots," as Benzer calls them in phage? If we interpret the discontinuities in function in terms of a linear DNA molecule, then we may well find that certain regions of a gene are "inert" when changed, since their code sequence is irrelevant to the product formed in respect to its role at certain specific times of development, but very relevant in respect to the interaction of this same product with other cellular components at a different stage of development. It would be interesting to see if the wing, bristle, eye, and lethal effects in the Notch region also show differences in the time of expression for these events.

In microorganisms there is also the paradox of genetic continuity in the absence of evidence of any intergenic overlapping in the chromosome maps, either in the linked regions of *Salmonella* or adjacent cistrons in phage. For these reasons it seems that all the structural aspects of both Lewis's and Pontecorvo's theories are not universally supported. Similarly, the functional aspects of both theories are not satisfied when a comparative outlook is adopted. How then should these various findings be interpreted?

A gene in *Drosophila* may be considered an integrated portion of the chromosome, a portion which affects one or more phenotypic characters. Its minimum length in terms of map units may be determined by the farthest distance observed between any two of its pseudoallelic members in a recombination test. The members of the series are functionally determined by their mutant expression in the trans or mutually heterozygous condition with that pseudoallele in the series which resembles the deficiency for the region. Mutation may or may not cause a total inactivation of the gene's function. The phenotype of a point mutation is the end-result of an abnormal gene-functioning which is caused by a very small alteration or lesion of the gene molecule and which affects the activity of the entire gene. The site altered by the mutation process may only cause the gene to lose a *part* of its function, in which case the trans situation between various independent mutations may occasionally show complementation (the wild phenotype). Such complementation depends on the functions altered by the mutations in the gene and is independent of the distance between the altered sites. Recombination may occur discontinuously *within* the gene at restricted regions. The cis-trans difference in pseudoallelic pairs can be considered a function

of the two genes involved; if both are altered the product in trans combination is mutant; if recombination reconstitutes the intact gene (which consequently is without altered sites), then the normal dominance of this gene over its recessive forms is reestablished and the wild phenotype results. The double mutant, carrying two altered sites, usually resembles the deficiency for the region, which, in the case of hypomorphic mutant series, is also that of the most extreme member.

A somewhat similar interpretation has been offered by Green (1958b). In his analysis of the white locus, Green rejects the possibility that the pseudoalleles are of a duplicate nature with related functions. The duplications of the Bar and Beadex-recessive cases indicate unequal crossing over as a common feature. Yet pseudoalleles are capable of very normal crossing over. This difference, according to Lewis (1958b), may reside in the fact that Bar, Beadex-recessive and the few other cases of unequal crossing over in *Drosophila melanogaster* represent cytological *tandem* repeats. However, true pseudoalleles would represent *reverse* repeats and hence would not show unequal crossing over. Duplications of hypomorphic mutations result in a more normal phenotype by the additive quantities of the functional products. Yet in pseudoalleles the double mutants involving hypomorphs result in a more exaggerated mutant expression. "Almost without exception, where two pseudoalleles are coupled to the same chromosome, the resultant phenotype is equivalent to and inseparable from that of the most extreme mutant recognized in the series." (The cases of Star and Stubble, however, indicate that in antimorphic mutations the most extreme mutant may be more extreme than its double mutant combinations. Hence it is more accurate to compare the double mutant to the deficiency for the region involved, since for Star and Stubble the double mutants and the deficiencies are similar in their reactions. This would eliminate the need for postulating intragenic suppressor activity in these two cases.) In Lewis's theory the duplication of the reverse type would have a concomitant position effect on the members resulting in a change of the normal dosage effects in hypomorphic mutants.

Green believes that the various pseudoallelic loci are involved in the production of a single product, probably an enzyme. "It is conceivable that each spatial locus contributes to the synthesis of the integrated product in a manner different from its neighbors. Specifically, each spatial locus may be concerned with the incorporation of a different moiety into the integrated whole and the cooperation of all loci is necessary before the product can be synthesized. In this meaning . . . each locus has a discrete function."

If we consider the gene as characterized for *Drosophila* and apply it to other complex loci, how valid is it? It should be stated that in such a comparison the various differences in genetic organization and in the adaptive mechanisms to life must be kept in mind before committing the error of generalizing the situation in one organism to that of all organisms. The most glaring contradiction so far is the apparent correspondence of complementation and functionally discrete units in molds. The complementation maps are approximately the same as those of the recombination maps. However, in some cases the supposed double or multiple mutations, which should be like deficiencies, show reverse mutation rates comparable with those of single mutants. Thus it is not an altogether proven case for the correspondence between the two mapping processes. It would be interesting to see how frequently these reverting multiple-function mutants are capable of recombination with the single-effect mutations in these series. This would indicate a similarity to the cases found for dumpy and Notch. As pointed out before this is exactly what was found in the histidinol dehydrogenase locus in *Salmonella*. It should also be possible to find allelic complementary trans mutants. This has been found for one sublocus in lozenge, and one case of interest involves a lozenge mutant complementary with some but not with all members of each of these classes of mutants.

If the correspondence of complementation and linkage mapping does hold, and an answer to this should not be long in the making, then the molds will be different in their gene function from that of the higher organisms represented by *Drosophila*. Pleiotropism in *Drosophila* might then be considered to occur as a secondary or later level of activity of gene products; whereas pleiotropism in the fungi would reflect functionally and spatially separate regions yielding complementation in trans compounds.

In viruses and bacteria the level of genetic organization is known to be different from that of cellular organisms; hence it is not too difficult to accept the existence of differences in gene action between them. The major differences lie in the degree of genetic continuity, which is practically complete in these microorganisms, but which shows an apparent internal segmentation in the Drosophila material. The prevalence of sequentially linked loci for biochemical syntheses in bacteria has not yet been found in the fungi or in the higher organisms, as far as it is possible to test for these reaction sequences. It is also easy to accept the existence of a unique metabolic system in *Salmonella* and other bacteria, inasmuch as the more complex cellular level of organization in higher organisms permits biochemical syntheses in extranuclear components of the cell.

The universality of gene conversion and other abnormalities of segregation of meiotic products is still open to further testing. No claim for their existence in *Drosophila* can be justified without meeting the rigorous criteria of techniques or controls to eliminate reverse mutation, linked suppressor mutations, negative interference, and genetic or environmental modifiers of the recombination process, as being the agents responsible for reported cases of double mutants or reversions without proper markers or, in the case of attached-X females, properly marked wild-type recombinations without the concomitant presence of reciprocally marked double mutants.

The evidence from maize indicates that "pseudoallelism," as defined from the *Drosophila* work, has not been demonstrated critically. The mechanisms seem to favor semi-allelic genes (true differentiated duplications) or synaptically equivalent regions analogous to the Bar case of *Drosophila*. In the case of the mammalian blood groups the evidence is indirect and highly debatable. In other multicellular forms only the beginnings of analysis have been accomplished, but are suggestive, especially in the *t*-series of mice.

CONCLUSION

In conclusion, the studies of complex loci are extremely valuable in enabling interpretations of gene structure and function to be made. The major interpretations offered do not, however, completely account for the comparative differences actually found in plant, animal, and microbial organisms. Yet the combined information does suggest a greater degree of basic similarity than of difference in the structure and functioning of the gene. According to the Watson-Crick theory of DNA structure, the nature of the genetic material in most organisms can be considered to be alike. Variations in the time of the DNA replication and the time of genetic recombination may account for the major differences in the structure of genes. The phylogenetic relationships of presently living organisms may determine their modes of gene functioning. The basic properties of genes to mutate, to respond to suppressors, or to alter their activities in the presence of genetic and environmental modifiers permit the geneticist to employ the same techniques in a variety of organisms; and differences in response should be carefully explored before they are considered to be unique. What is most important, however, for the geneticist, is to recognize a need for studying the comparative genetics of his problem. Without it he falls into the age-old error of viewing the macrocosm through the limited perspective of a microcosm.

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LIST OF LITERATURE

Agol, I. J. 1931. Step allelomorphism in *Drosophila melanogaster*. *Genetics*, 16: 254–266.

Barish, N., and A. S. Fox. 1956. Immunogenetic studies of pseudoallelism in *Drosophila melanogaster*. II. Antigenic effects of the vermilion pseudoalleles. *Genetics*, 41: 45–57.

Beadle, G. W. 1945. Genetics and metabolism in *Neurospora*. *Physiol. Rev.*, 25: 643–663.

——, and B. Ephrussi. 1936. The differentiation of eye pigments in Drosophila as studied by transplantation. *Genetics*, 21: 225–247.

——, and E. L. Tatum. 1941. Genetic control of biochemical reactions in *Neurospora*. *Proc. Nat. Acad. Sci., Wash., 27:* 499–506.

Bender, H. A., and R. C. King. 1958. Studies on the expression of various *singed* alleles in *Droso-*

phila melanogaster. *Proc. 10 int. Congr. Genet.*, Montreal, 1958, 2: 21.

BENZER, S. 1957. The elementary units of heredity. In *The Chemical Basis of Heredity*, (W. D. McElroy and B. Glass, eds.), pp. 70–93. Johns Hopkins Press, Baltimore.

——, and E. FREESE. 1958. Induction of specific mutations with 5-bromouracil. *Proc. nat. Acad. Sci., Wash.*, 44: 112–119.

BONNER, D. 1956. The genetic unit. *Cold Spr. Harb. Symp. quant. Biol.*, 21: 163–170.

BLANC, R., and G. CHILD. 1937. Reversal of dominance in the dumpy locus in *D. melanogaster*. *Drosophila Inform. Serv.*, 8: 73.

BRIDGES, C. B. 1936. Bar as a duplication. *Science*, 83: 210–211.

BRINK, R. A. 1958. The genetic basis of a transallelic change occurring invariably in certain maize heterozygotes. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 34–35.

CARLSON, E. A. 1957. A further analysis of allelism in *D. melanogaster*. *Genetics*, 42: 363.

——. 1958a. Some problems involving the *cis-trans* effect in *Drosophila*. *Proc. 10 int. Congr. Genet.*, Montreal, 1958, 2: 43.

——. 1958b. Allelism, complementation, and pseudoallelism at the dumpy locus in *D. melanogaster*. Ph.D. thesis, 1958, Indiana University, Bloomington, Ind. *Genetics*, in press.

——. 1958c. The bearing of a complex locus in *Drosophila* on the interpretation of the Rh series. *Amer. J. Hum. Genet., 10:* 465–473.

CASE, M. E. 1958. Linear relationships of allelic mutants at the *Pan-2* locus in *Neurospora crassa*. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 45.

——, and N. H. GILES. 1958. Evidence from tetrad analysis for both normal and aberrant recombination between allelic mutants in *Neurospora crassa*. *Proc. nat. Acad. Sci., Wash.*, 44: 378–390.

CHILD, G. P. 1935. Phenogenetic studies on scute-1 of *Drosophila melanogaster*. I. The associations between the bristles and the effects of genetic modifiers and temperature. II. The temperature effective period. *Genetics*, 20: 109–126; 127–155.

CHOVNICK, A. 1958a. Aberrant segregation and pseudoallelism at the garnet locus in *Drosophila melanogaster*. *Proc. nat. Acad. Sci., Wash.*, 44: 333–337.

——. 1958b. Structural and functional aspects of pseudoallelism in *Drosophila melanogaster*. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 49.

——, and R. J. LEFKOWITZ. 1956. A phenogenetic study of the lozenge pseudoalleles in *Drosophila melanogaster*. I. Effects on the development of the tarsal claws in homozygotes. *Genetics*, 41: 79–92.

——, and A. S. FOX. 1956. A phenogenetic study of the lozenge pseudoalleles in *Drosophila melanogaster*. II. Effects on the development of tarsal claws in heterozygotes. *Genetics*, 41: 589–604.

COE, E. H., JR. 1958. A continuing, non-reverting conversion-type phenomenon at the *B* locus in maize. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 55.

DEMEREC, M. 1928. The behavior of mutable genes. *Proc. 5. int. Congr. Genet.*, Berlin, 1927, 1: 183–193.

——. 1954. What is a gene—twenty years later. *Amer. Nat.*, 89: 5–20.

——. 1956. A comparative study of certain gene loci in *Salmonella*. *Cold Spr. Harb. Symp. quant. Biol.*, 21: 113–122.

——, I. BLOMSTRAND, and Z. E. DEMEREC. 1955. Evidence of complex loci in *Salmonella*. *Proc. nat. Acad. Sci., Wash.*, 41: 359–364.

DOBZHANSKY, T. 1930. The manifold effects of the genes *Stubble* and *stubbloid* in *Drosophila melanogaster*. *Z. ind. Abst. Vererblehre*, 54: 719–746.

DUBININ, N. P. 1933. Step allelomorphism in *Drosophila melanogaster*. *J. Genet.*, 443–464.

——, and B. N. SIDOROV. 1934. Relation between the effect of a gene and its position in the system. *Amer. Nat.*, 68: 377–381.

——, N. SOKOLOV, and G. TINIAKOV. 1937. Crossing over between the genes yellow, achaete, and scute. *Drosophila Inform. Serv.*, 8: 76.

DUNN, L. C. 1956. Analysis of a complex gene in the house mouse. *Cold Spr. Harb. Symp. quant. Biol.*, 21: 187–196.

EDGAR, R. S. 1958. Phenotypic properties of heterozygotes in the bacteriophage T4. *Genetics*, 43: 235–248.

FISHER, R. A. 1946. The fitting of gene frequencies to data on rhesus reactions. *Ann. Eugen., Lond.*, 13: 223–224.

FOX, A. S., and A. CHOVNICK. 1954. Immunogenetic studies of the *lozenge* pseudoalleles in *Drosophila melanogaster*. *Proc. 9. int. Congr. Genet.*, Bellagio, 1953, 2: 817.

GLASS, H. B. 1933. A new allelomorphic compound presenting the phenotype of the wild *Drosophila melanogaster*. *J. Genet.*, 27: 233–241.

——. 1949. The genes and gene action. *Surv. Biol. Progr.*, 1: 15–57.

GOLDSCHMIDT, R. 1955. Theoretical Genetics. University of California Press, Berkeley.

GREEN, M. M. 1954. Pseudoallelism at the vermilion locus in *Drosophila melanogaster*. *Proc. nat. Acad. Sci., Wash.*, 40: 92–99.

——. 1955a. Pseudoallelism and the gene concept. *Amer. Nat.*, 89: 65–71.

——. 1955b. Phenotypic variation and pseudoallel-

ism at the forked locus in *Drosophila melanogaster*. *Proc. nat. Acad. Sci., Wash.*, 41: 375–379.

——. 1958a. On the occurrence of non-homologous pairing and crossing over in *Drosophila*. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 104.

——, and K. C. Green. 1956. A cytogenetic analysis of the lozenge pseudoalleles. *Z. ind. Abst. Vererblehre*, 87: 708–721.

Hartman, P. E. 1956. Linked loci in the control of consecutive steps in the primary pathway of histidine synthesis in *Salmonella typhimurium*. *Carnegie Inst. Wash. Publ.*, 612, Genetic Studies with Bacteria; pp. 35–62.

——. 1957. Transduction: a comparative review. In *The Chemical Basis of Heredity*. (W. D. McElroy and B. Glass, eds.), pp. 408–462. Johns Hopkins Press, Baltimore.

——, Z. Hartman, D. Serman, and J. Loper. 1958. Genetic complementarity in histidineless *Salmonella typhimurium*. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 115.

Hexter, W. M. 1957. Genetic resolution in *Drosophila*. *Genetics*, 42: 376.

——. 1956. Pseudoallelism at the *g* locus. *Drosophila Inform. Serv.*, 30: 121.

——. 1958a. Probable gene conversion in *Drosophila*. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 120.

——. 1958b. On the nature of the garnet locus in *Drosophila melanogaster*. *Proc. nat. Acad. Sci., Wash.*, 44: 768–771.

Horowitz, N. H. 1950. Biochemical genetics of *Neurospora*. *Advanc. Genet.*, 3: 33–71.

Ives, P. T., and D. T. Noyes. 1951. A study of pseudoallelism in two multiple allelic series in *Drosophila melanogaster*. *Anat. Rec.*, 111: 149.

Judd, B. H. 1958. An analysis of the subdivisions of the white region in *Drosophila melanogaster*. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 137.

Komai, T. 1950. Semi-allelic genes. *Amer. Nat.*, 84: 381–392.

Lacy, A. M., and D. M. Bonner. 1958. Complementarity between alleles and the *Td* locus in *Neurospora crassa*. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 157.

Laughnan, J. R. 1955. Structural and functional bases for the action of the *A* alleles in maize. *Amer. Nat.*, 89: 91–103.

Lederberg, E. 1958. Fine structure of the *Gal* loci in *Escherichia coli* K-12. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 161–2.

Lewis, E. B. 1941. Another case of unequal crossing over in *Drosophila melanogaster*. *Proc. nat. Acad. Sci., Wash.*, 27: 31–34.

——. 1942. The Star and asteroid loci in *Drosophila melanogaster*. *Genetics*, 27: 153–154.

——. 1945. The relation of repeats to position effect in *Drosophila melanogaster*. *Genetics*, 30: 137–166.

——. 1948. Pseudoallelism in *Drosophila melanogaster*. *Genetics*, 33: 113.

——. 1950. The phenomenon of position effect. *Advanc. Genet.*, 3: 73–115.

——. 1951. Pseudoallelism and gene evolution. *Cold Spr. Harb. Symp. quant. Biol.*, 16: 159–174.

——. 1952. The pseudoallelism of white and apricot in *Drosophila melanogaster*. *Proc. nat. Acad. Sci., Wash.*, 38: 953–961.

——. 1954a. The theory and application of a new method of detecting chromosomal rearrangements in *Drosophila melanogaster*. *Amer. Nat.*, 88: 225–239.

——. 1954b. Pseudoallelism and the gene concept. *Caryologia*, suppl. vol., 100–105.

——. 1955. Some aspects of position pseudoallelism. *Amer. Nat.*, 89: 73–89.

——. 1956. An unstable gene in *Drosophila melanogaster*. *Genetics*, 41: 651.

——. 1957. Two wings or four? *Engineering and Science Monthly*, Cal. Tech., Nov. 1957.

Lindegren, C. C. 1953. Gene conversion in *Saccharomyces*. *J. Genet.*, 51: 625–647.

——, and D. D. Pittman. 1958. Recombination in a complex locus in *Saccharomyces*. *Proc. 10. int. Congr. Genet.*, Montreal, 25 August, 1958, suppl. to vol. 2.

McClintock, B. 1944. The relation of homozygous deficiencies to mutations and allelic series in maize. *Genetics*, 29: 478–502.

MacKendrick, M. E., and G. Pontecorvo. 1952. Crossing over between alleles at the *w* locus in *Drosophila melanogaster*. *Experientia*, 8: 390–394.

Mitchell, H. K. 1957. Crossing over and gene conversion in *Neurospora*. In *The Chemical Basis of Heredity* (W. D. McElroy and B. Glass, eds.), pp. 94–113. Johns Hopkins Press, Baltimore.

Morgan, T. H. 1926. *The Theory of the Gene*, p. 25. Yale Univ. Press, New Haven.

Muller, H. J. 1919. A series of allelomorphs in *Drosophila* with non-quantitative relationships. Read before the Amer. Soc. of Naturalists, Princeton, 31 Dec. 1919. Title in *Science*, 51: 171 (1920).

——. 1922. Variation due to change in the individual gene. *Amer. Nat.*, 56: 32–50. (Read before Amer. Soc. of Naturalists, Toronto, 29 Dec. 1921.)

——. 1928. The problem of genic modification. *Proc. 5. int. Congr. Genet.*, Berlin, 1927, *Z. ind. Abst. Vererblehre*, suppl. I, 234–260.

——. 1932. Further studies on the nature and causes of gene mutations; (see section, "multiple allelomorphs forming non-quantitative series").

Proc. 6. int. Congr. Genet., Ithaca, 1932, 1: 213–255.

——. 1935a. The position effect as evidence of the localization of the immediate products of gene activity. *Summ. Commun. XV Int. Physiol. Congr.* (Lenin-Mosc.), 286–289.

——. 1935b. The origination of chromatin deficiencies as minute deletions subject to insertion elsewhere. *Genetics*, 17: 237–252.

——. 1935c. On the incomplete dominance of the allelomorphs of white in *Drosophila melanogaster*. *J. Genet.*, 30: 407–414.

——. 1936. *Bar* duplication. *Science*, 83: 528–530.

——. 1956. On the relation between chromosome changes and gene mutation. *Mutation, Brook. Symp. Biol.*, 8: 126–146.

——, and I. I. Oster. 1957. Suppressor action effective with a subgene deficiency of a normally duplicated locus. *Drosophila Inform. Serv.*, 31: 141.

——, and A. Prokoveyeva. 1935. Continuity and discontinuity of the hereditary material (the individual gene in relation to the chromomere and the chromosome). *Proc. nat. Acad. Sci., Wash.*, 21: 16–26.

——, A. A. Prokoveyeva-Belogovskaya, and K. V. Kossikov. 1936. Unequal crossing over in the *Bar* mutant as a result of duplication of a minute chromosomal section. *C. R. Acad. Sci. U.S.S.R.*, 2: 78.

Nelson, O. E., Jr. 1958. Intercrosses among alleles at the *Waxy* locus in maize. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 204.

Offermann, C. A. 1935. The position effect and its bearing on genetics. *Bull. Acad. Sci. U.S.S.R.*, 89: 129–152.

Oliver, C. P. 1940. A reversion to wild type associated with crossing over in *Drosophila melanogaster*. *Proc. nat. Acad. Sci., Wash.*, 452–453.

——, and M. M. Green. 1944. Heterosis in compounds of lozenge alleles in *Drosophila melanogaster*. *Genetics*, 29: 331–347.

Panshin, I. B. 1935. New evidence for the position effect hypothesis. *C. R. Acad. Sci. U.S.S.R.*, 4: 85–88.

Pontecorvo, G. 1952. Genetic formulation of gene structure and gene action. *Advanc. Enzymol.*, 13: 121–149.

——. 1955. Gene structure and action in relation to heterosis. *Proc. roy. Soc. B.*, 144: 171–177.

——. 1956. Allelism. *Cold Spr. Harb. Symp. quant. Biol.*, 21: 171–174.

——. 1958. *Trends in Genetic Analysis*. Columbia University Press, New York.

——, and J. A. Roper. 1956. Resolving power of genetic analysis. *Nature, Lond.*, 178: 83–84.

Pritchard, R. H. 1955. The linear arrangement of a series of alleles of *Aspergillus nidulans*. *Heredity*, 9: 343–371.

——. 1958. Recombination and negative interference in *Aspergillus nidulans*. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 223–224.

Race, R. C., and Sanger, R. 1954. *Blood Groups in Man*, 2nd ed. Charles C Thomas, Springfield, Ill.

Roman, H. 1956. Studies of gene mutation in *Saccharomyces*. *Cold Spr. Harb. Symp. quant. Biol.*, 21: 175–186.

Roper, J. A. 1950. Search for linkage between genes determining a vitamin requirement. *Nature, Lond.*, 166: 956.

Serebrovsky, A. S. 1930. Untersuchungen über Treppenallelomorphismus IV. Transgenation scute-6 und ein Fall des "Nicht-Allelomorphismus" von Gliedern einer Allelomorphenreihe bei *Drosophila melanogaster*. *Arch. EntwMech. Org.*, 122: 88–104.

Skaar, P. D., and H. Davidson. 1956. Discussion following M. Demerec's paper. *Cold Spr. Harb. Symp. quant. Biol.*, 21: 120.

Slatis, H. M., and D. A. Willermet. 1954. The miniature complex in *Drosophila melanogaster*. *Genetics*, 39: 45–58.

St. Lawrence, P., and D. M. Bonner. 1957. Gene conversion and problems of allelism. In *The Chemical Basis of Heredity* (W. D. McElroy and and B. Glass, eds.), pp. 114–122. Johns Hopkins Press, Baltimore.

Stadler, L. J. 1954. The gene. *Science*, 120: 811–819.

——, and M. Emmerling. 1956. Relation of unequal crossing over to the interdependence of R^r *elements* (*P*) and (*S*). *Genetics*, 41: 124–137.

——, and M. G. Nuffer. 1953. Problems of gene structure II. Separation of R^r elements (*S*) and (*P*) by unequal crossing over. *Science*, 117: 471–472.

Stephens, S. G. 1948. A biochemical basis for the pseudoallelic *anthocyanin* series in *Gossypium*. *Genetics*, 33: 191–214.

——. 1952. "Homologous" genetic loci in *Gossypium*. *Cold Spr. Harb. Symp. quant. Biol.*, 16: 131–141.

Stormont, C. 1955. Linked genes, pseudoalleles, and blood groups. *Amer. Nat.*, 89: 105–116.

Streisinger, G., and N. Franklin. 1956. Mutation and recombination at the host range genetic region of phage T2. *Cold Spr. Harb. Symp. quant. Biol.*, 21: 103–112.

Sturtevant, A. 1925. The effects of unequal crossing over at the Bar locus in *Drosophila*. *Genetics*, 10: 117–147.

——, and J. Schultz. 1931. The inadequacy of the

subgene hypothesis of the nature of the *scute* allelomorphs of *Drosophila*. *Proc. nat. Acad. Sci., Wash.*, 17: 265–270.

SUSKIND, S. R. 1957. Gene function and enzyme formation. In *The Chemical Basis of Heredity* (W. D. McElroy and B. Glass, eds.), pp. 123–128. Johns Hopkins Press, Baltimore.

TSUJITA, M. 1955. On the crossing over between E^{k} and E^{Kp} of the *E* allelic series in the silkworm. *Jap. J. Genet.*, 30: 227–235.

WEIJER, J. 1958. Evidence for a complex structure of the *Td* locus in *Neurospora crassa*. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 310.

WELSHONS, W. J. 1958a. A preliminary investigation of pseudoallelism at the Notch locus of *Drosophila melanogaster*. *Proc. nat. Acad. Sci., Wash.*, 44: 254–258.

——. 1958b. Pseudoallelic recessive lethals at the Notch locus of *Drosophila melanogaster*. *Proc. 10. int. Congr. Genet.*, Montreal, 1958, 2: 311–312.

——. 1958c. The analysis of a pseudoallelic recessive lethal system at the Notch locus of *Drosophila melanogaster*. *Cold Spr. Harb. Symp. quant. Biol.*, (in press).

WIENER, A. S. 1954. *Rh-Hr Blood Types*. Grune and Stratton, New York.

WOODWARD, D. O. 1958. Heterokaryon complementation between adenyl succinaseless mutants of *Neurospora crassa*. *Proc. 10. int. Congr. Genet.*, Montreal, 2: 321.

YANOFSKY, C., and D. BONNER. 1955. Gene interaction in tryptophan synthetase formation. *Genetics*, 40: 761–766.

——. 1958. Restoration of tryptophan synthetase activity in *Escherichia coli* by suppressor mutations. *Science*, 128: 843–844.

YU, P. Y., and T. S. CHANG. 1948. Further studies on the inheritance of anthocyanin pigmentation in Asiatic cotton. *J. Genet.*, 49: 46–56.

ZINDER, N. D., and J. LEDERBERG. 1952. Genetic exchange in *Salmonella*. *J. Bact.*, 64. 679–699.

NEW BIOLOGICAL BOOKS

The aim of this department is to give the reader brief indications of the character, the content, and the value of new books in the various fields of Biology. In addition there will occasionally appear one longer critical review of a book of special significance. Authors and publishers of biological books should bear in mind that THE QUARTERLY REVIEW OF BIOLOGY *can notice in this department only such books as come to the office of the editor. The absence of a book, therefore, from the following and subsequent lists only means that we have not received it. All material for notice in this department should be addressed to H. B. Glass, Editor of* THE QUARTERLY REVIEW OF BIOLOGY, *Department of Biology, The Johns Hopkins University, Baltimore 18, Maryland, U. S. A.*

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GENERAL BIOLOGY: PHILOSOPHY AND EDUCATION

THE FOUNDATIONS OF LIFE SCIENCE.

By Mark Graubard. D. Van Nostrand Company, Princeton, Toronto, London, and New York. $6.50. xii + 627 pp.; ill. 1958.

This book is said to be "for students who do not major in science." It is freshly conceived, well written, and should prove to be a major contribution to the area of general education. The book provides a historical perspective of biological concepts by discussing their development in the minds of the individuals who gave them their shape and substance. There is a commendable use of authoritative and original sources, and the plates and figures are selected specifically for this book. Each chapter has lists of well-chosen references to encourage the student further in each area.

The approach is not one of superficial simplification. A careful selection of technical material has been made in most of the major areas to verify the concepts presented, and the scope of these generalizations is made clear. The degree of dependability of the scientific quest is demonstrated by this approach, which also allows the author to lead the student into the open ends of unresolved questions whose solutions lie ahead.

In my own opinion, the book should be expanded to give more treatment to ecology and man's place in nature. These are areas that deserve more consideration, particularly for the non-major student. If the author's accurate, interesting narrative style were to cover these additional areas with the same success, this book could be recommended to an even greater non-scientific audience.

DAVID G. BARRY

THE PHYSICIST'S CONCEPTION OF NATURE.

By Werner Heisenberg; translated from the German by Arnold J. Pomerans. Harcourt, Brace & Company, New York. $3.75. 192 pp. 1958.

The Physicist's Conception of Nature consists of a rather heterogeneous series of writings: an essay on The Idea of Nature in Contemporary Physics, another on Atomic Physics and Causal Law, and a third on Classical Education, Science and the West. The remaining portion of the book, entitled Historical Sources, is composed principally of quotations from the works of scientists and philosophers from Kepler

to de Broglie; these are allocated to three chapters entitled in turn The Beginnings of Modern Science, The Origins of the Mechanistic and Materialist World-View, and The Crisis of the Mechanistic-Materialist Conception. The quotations chosen are of consummate interest in themselves, but it is not made wholly clear how they are intended to relate to the rest of the content of the volume. The section on historical sources (which includes them) begins: "In this essay I have tried to give a brief sketch of the philosophical problems that have arisen out of changes in the world-view of physics and science." Since the section so beginning follows the essays on classical education, atomic physics, and causal law and is separated by 40 pages from the section on the idea of nature in contemporary physics, which in any case deals with contemporary, not with historical, ideas, the reader is left to wonder whether the cross reference designates something not included in the volume. The quotations, elegant as they are, require more mortar to mold them together into a cohesive edifice than they are allotted here. The essay on classical education, somewhat autobiographical, will be of particular interest to those who are curious as to the sources and stimulations for Heisenberg's own ideas. The most interesting essay in the volume is the first, on The Idea of Nature in Contemporary Physics. Its principal tenet is that "when we speak of the picture of nature in the exact science of our age, we do not mean a picture of nature so much as a *picture of our relationships with nature*. . . . Science is now focussed on the network of relationships between man and nature, on the framework which makes us as living beings dependent parts of nature, and which we as human beings have simultaneously made the objects of our thoughts and actions. Science no longer confronts nature as an objective observer, but sees itself as an actor in this interplay between man and nature." Elsewhere he puts it more succinctly, "Modern man confronts only himself." The essay is cogently argued, and lucidly expressed. Like the rest of the book, it will be found eminently readable by the readers of the *Quarterly Review of Biology*, and it is to such as they that it is addressed.

JANE OPPENHEIMER

BIOLOGY: HISTORY AND BIOGRAPHY

LOUIS PASTEUR. *A Great Life in Brief. By Pasteur Vallery-Radot; translated from the French by Alfred Joseph. Alfred A. Knopf, New York.* $3.00. x + 210 pp. 1958.

The author of this short biography is the grandson and, he tells us in the Foreword, the last descendant of the great scientist. Born in 1886, he has been Professor of Medicine in the University of Paris since 1929. He is the son of Pasteur's daughter by René Vallery-Radot, a professional writer and author of the famous biography of Louis Pasteur. The grandson has previously edited Pasteur's *Oeuvres complètes* and his *Correspondance* and has written two short biographical works on Pasteur in French.

One of a series of short biographies, this book and a life of Darwin are the only ones devoted to scientists. Translation from the French has had no apparent deleterious effects. Rich in anecdote, the story moves smoothly and engagingly through the life of its subject. The logical sequence in Pasteur's work—from crystallography to immunization—is one of the themes and is well demonstrated.

The book will be useful to recommend to readers who are staggered by the thought of undertaking René Vallery-Radot's more formidable classic. It is however doubtful that any important new light is cast on the genius of Pasteur.

VICTOR A. MCKUSICK

DISEASE, LIFE, AND MAN. *Stanford Studies in the Medical Sciences, IX. Selected Essays by Rudolf Virchow; translated and with an introduction by Lelland J. Rather. Stanford University Press, Stanford.* $5.00. x + 273 pp. 1958.

Disease, Life, and Man presents translations of ten semi-philosophical articles and lectures by Virchow on medicine, pathology, and biology. The original German texts appeared between the years 1847 and 1898. Since only a few have previously been published in English, it may perhaps be of some advantage to have them bound within a single cover for the benefit of students not fortunate enough to be able to read them in German.

The particular essays chosen revolve their arguments principally around the concepts that disease results from deviations of normal functions, that both normal and deviant functions of life must always be referred to the cell, and that the cell is the basis of the unity of life in all living things. While the title is accurate, in that the selections refer to disease, to life, and to man more than might be true of the writings of many other authors, they do not reflect the full breadth of Virchow's interest in man, and his anthropological, archeological, epidemiological, and politico-social interests are scarcely touched upon. This choice has been deliberate on the part of the translator, and is probably appropriate, since cellular pathology was of course central in Virchow's thought. The essays selected are, however, especially interesting in their revelation of the depth to which Virchow's own insights were historically oriented.

Such were Virchow's power and penetration of thought and so revitalizing were his ideas for medicine that it is easy to lapse into the error of expect-

ing his writings to read like those written by his successors several generations later. Yet the articles presented here sound unexpectedly dated. A question arises as to whether this may be bound up with the translation, which is certainly faithful, but not always fluid. "All knowledge of facts is historical, not only because the facts are discovered by observations made prior to their application in newly arranged experiments, but also because one knows accurately only what one knows historically. The naked facts are doubtful weapons." Virchow's words are reproduced, but somehow his style of thinking fails to come through.

The notes are brief, and those referring to the translated articles represent mainly a biographical glossary. A short list is appended of the German titles and the original German sources of the translated articles. The occasions on which the articles were written or the lectures delivered are not systematically recorded.

JANE OPPENHEIMER

THE YOUNG NATURALIST

A SCIENTIST OF TWO WORLDS: LOUIS AGASSIZ.
By Catherine Owens Peare. J. B. Lippincott Company, Philadelphia and New York. $3.00. 188 pp. + 1 pl. 1958.

A biography of Louis Agassiz, this book is one of a series which, according to its jacket, proposes "to acquaint young people with outstanding individuals of different races, cultures and creeds." What was outstanding in Agassiz's individuality was not that his life bridged two worlds, but that his thought grasped the world of life as one whole. Miss Peare's biography is successful in so far as it portrays Agassiz's dedication to his labors, and a moral is continuously to be drawn as to the procedures, vicissitudes, and rewards of the life of a scientist. For the sake of the young reader the story is slightly but not opprobriously fictionalized by the addition of hypothetical, if possible, conversations. Yet the moral is more pointed than the tale adorned. Virginia Woolf wrote over forty years ago of some of the books we read in childhood that they "have something of the unreality and awfulness of a stolen sight of the dawn coming over quiet fields when the household is asleep." It is dubious whether this biography heralds the dawns of any frightening new insights. It casts the ordinary light of day, true, without distorting shadows, on the life of its subject. Since he was extraordinary, it may prove stimulating to some young readers, and it is to be hoped that it may draw them to look deeper into Agassiz's thought.

JANE OPPENHEIMER

ECOLOGY AND NATURAL HISTORY

A TREATISE ON LIMNOLOGY. *Geography, Physics, and Chemistry. Volume 1.*
By G. Evelyn Hutchinson. John Wiley & Sons, New York; Chapman & Hall, London. $19.50. xiv + 1015 pp. + 9 pl.; text ill. 1957.

In this volume and the one to follow Hutchinson has attempted the monumental task for one man of giving "as complete an account as is possible of the events characteristically occurring in lakes." He has not only synthesized a voluminous world literature in the field, and leavened it by personal field experience on four continents and by personal contact with many of the researchers in limnology and cognate fields, but he has also included many hitherto unpublished data from various sources. As a mature and authoritative summary of the subject, the book has no equal in the world literature. Already it has taken its place as one of the "classics" in the field, indispensable to every serious limnologist.

This first volume consists of 17 chapters, describing the origin of lake basins and their morphometry, the properties of water as a substance, currents and waves in lakes, and the optical and thermal properties of lakes. The last ten chapters contain detailed discussions of the various substances in water that comprise the chemical environment of aquatic organisms—dissolved oxygen, the carbon-dioxide complex and hydrogen-ion concentration, redox potential and the ion cycle, phosphorus, sulfur, silica, minor metallic elements, nitrogen, and organic matter. In these chapters Hutchinson's great interest in biogeochemistry is evident. The organisms themselves and their interrelations with the chemico-physical environment are to be discussed in the second volume.

Wherever possible, the physical and chemical processes are formulated mathematically. Definitions of the symbols used are contained in an appendix. General adoption and use of these symbols by limnologists will simplify discussion and obviate misinterpretation. For the untrained reader each chapter is followed by a non-technical summary. All persons with any interest in the dynamics of lakes will find much stimulating material in this book, interestingly written, and authoritatively presented.

D. G. FREY

MARINE ECOLOGY.
By Hilary B. Moore. John Wiley & Sons, New York; Chapman & Hall, London. $9.50. xii + 493 pp.; ill. 1958.

This book starts with a short chapter containing a discussion of the literature of marine ecology, fol-

lowed by some remarks on the differences between autecology and synecology and a very brief mention of a few ecological methods. The next three chapters consider successively the physical, chemical, and biological environmental factors. These are followed by two chapters which outline the properties of the habitats found in the ocean. The next five chapters take up the characteristics of marine organisms, classified according to habitat. There is a final review chapter in which the complexities resulting from interactions between many factors, the regularities observed in the functional composition of communities, and the dynamic nature of communities are briefly discussed. One result of this method of organizing the book is a good deal of repetition; e.g., the relation between the shell color of *Purpura* and its food is referred to in at least six different places. Another result is an underemphasis on the general problems of productivity, population structure, and control and the processes operative in communities. These subjects are all mentioned, and in certain special cases are considered in some detail, but there is no general critical review of all the information and conflicting viewpoints on any one of them.

The author states that the book has been written "from the special point of view of the needs of a student in the field." The word "field" is open to two interpretations; it may mean the natural habitats within which work is done or it may mean the subject, ecology. If the first meaning is taken, it is hard to see how the book would be very useful in the field, for the coverage of methods is minimal and there is no critical discussion of sampling problems, which are at the heart of all field work. If the second meaning is correct, the book does not seem particularly suitable as a student textbook in marine ecology, because it includes much detail, but very little generalization. This detail plus the extensive bibliography might suggest that the volume would be suitable as a source book for advanced students, but its admitted emphasis on English-language publications is a definite limitation in this regard.

The book has many characteristics of a hastily written and published volume: a total of 11 typographical and other errors, found on a random sample of 40 pages, confirms the general impression of frequent errors; in an apparent attempt to simplify, the captions under some figures have been reduced to such an extent that parts of the figure are understandable only by reference to the original publication; the names of a number of well-known authors are misspelled. One serious misstatement should be noted (pp. 83, 130): glycogen can never serve as "an oxygen supply" though it can be used as an energy source under anaerobic conditions; the latter is presumably what the author means.

The book would have gained a great deal if the sections had been more carefully organized. To give only one example, in successive paragraphs of one section the following subjects are discussed: upwelling, nutrients, and phytoplankton production; the *Sargassum* community; areas of mixing and phytoplankton production; the diurnal migration of zooplankton; the natural history of whales; and the resistance of whales to caisson disease. These may all be appropriate to a discussion of the Upper Oceanic Zone, but they give the impression of a series of interesting but somewhat disconnected comments on a general theme rather than one of an integrated picture of the subject. This is unfortunate, for the author is aware that marine ecology suffers "from the overcollection of data to the point where the mass of material tends to become indigestible," and he emphasizes the need for "more reviewing and coordinating of the existing information."

E. W. Fager

Perspectives in Marine Biology. *Symposium held at Scripps Institution of Oceanography, University of California, March 24–April 2, 1956.*

Edited by A. A. Buzzati-Traverso. University of California Press, Berkeley and Los Angeles. $10.00. xvi + 621 pp. + 1 folded chart; ill. 1958.

Certain aspects of the symposium held in 1956 at La Jolla have made it famous, and publication of this volume has been impatiently awaited by interested bystanders. Little of the fringe benefits (if such they may be called) of the conference are recorded in this book, which contains the formal papers presented and much of the commentary "from the floor" (much of it unsaid at the time and submitted in writing later). The cerebration sections or "idea" groups and the final peroration by a panel are for the most part unreported, although their consensus is summarized at the end. This volume includes many useful and informative papers, some of them frequently cited as being "in press" since the time of their presentation. The papers range from general "think" pieces to critical presentations of recent investigations, by a veritable galaxy of authors in many fields of biology. These include Zengevich, Thorson, Wieser, Riedl, and Drach on ecological aspects; Tonolli, Bogorov, Hardy Rohde, and Margalef on plankton problems; Baldwin, Guzman Barron, Szent-Györgyi, Pittendrigh, Bullock, and others on physiological matters; Thorpe and Miyadi on behavior; Yonge on corals; and so on. With such rich fare, the effort of Buzzati-Traverso to summarize what it all means for the future of marine biology is inevitably anticlimactic. The volume is, in short, a rare and rich smörgasbord, and the reader will have to judge what suits his palate best.

Joel W. Hedgpeth

WOODLAND ECOLOGY.

By Ernest Neal. Harvard University Press, Cambridge. $1.75. xii + 117 pp. + 8 pl.; text ill. 1958.

An inexpensive and concise review, this little book seems intended to serve as an introduction to different phases of forest ecology for high school students and first year college classes. Although apparently written for conditions in England (that this is originally an English publication is nowhere stated), the descriptions are in such general terms as to make them fit also for eastern North America, and the details concerning apparatus and methods are universal. The book gives compendious information on how to make observations on different aspects of the vegetation and the habitat factors in a wood, and also on the main animals, their habitats, food cycles, food relationships, and methods of finding them, to mention but a few of the many themes the author has been able to pack into so small a volume. A number of simple drawings explain some aspects discussed in the text, and some good, informative plates help to make the reading pleasant. Neal's expressions are clear and exact, and the entire text is such that few other books of its character are as suitable to increase the interest in nature study among young and prospective naturalists.

ÁSKELL LÖVE

SPIDERS, SCORPIONS, CENTIPEDES AND MITES. *The Ecology and Natural History of Woodlice, Myriapods, and Arachnids.*

By J. L. Cloudsley-Thompson. Pergamon Press, New York, London, Paris, and Los Angeles. $9.00. xiv + 228 pp. + 35 pl.; text ill. 1958.

This book is intended as a reference guide to the various, and mostly little-known, land arthropods enumerated in the title and subtitle. About some of these creatures even simple, basic facts are hard to come by because of the sparse, scattered, and inadequate literature. Whereas these animals have been arbitrarily selected, and exemplify the special interests of the author, they live largely in and on the soil layer of the British Isles and comparable areas of the world.

Each group is considered in a well-rounded chapter. Satisfactory discussions are presented on their classification and distribution, general behavior, food and feeding habits, enemies, reproduction, and life cycles. Appended to each chapter is a selected bibliography with pertinent biological and identification references. The plates and text figures give typical portrayals of the several distinctive classes.

The author's approach is that of a naturalist who emphasizes the ecology, physiology, and life histories of his subjects. He presents the known facts and suggests some of the problems remaining to be solved. Much of the information is original, for the author has been an active investigator for many years. Whereas the book is British in flavor and is largely preoccupied with that fauna, its broad scope makes it an invaluable reference work for all students.

WILLIS J. GERTSCH

EVOLUTION

FOSSIL MEN.

By Marcellin Boule and Henri V. Vallois; translated by Michael Bullock. The Dryden Press, New York. $9.50. xxvi + 535 pp.; ill. 1957.

This is the English translation of the fifth edition of the late Marcellin Boule's *Les Hommes Fossiles*, first published in 1921. The last previous edition, the fourth, appeared in 1952.

The text has been brought up to date by the inclusion of recent discoveries, such as those made at Saldanha in 1953, at Ternifine in 1954, and at Swanscombe in 1955. Similarly, the Piltdown discovery of 1953—that this Sussex monster was a fraud—is considered in detail.

In general, the presentation is authoritative and conservative in point of view. Unfortunately, however, it often adheres too closely to the original, but of necessity somewhat antiquated, Bouleian version of nearly four decades ago. Thus, one encounters such archaisms as a semi-erect Neanderthal man, the labeling of Rhodesian man as a Neanderthalian, and the allocation of *Oreopithecus* to the Old World monkeys. Similarly, in discussing the phylogeny of the modern type of man, one finds the pathological, hence enigmatic, Kanam jaw presented as an undoubted early Pleistocene specimen of *Homo sapiens*. Notwithstanding these defects, this book, considered as a whole, is a sound one. It continues to be one of the few really good volumes that deal with fossil man.

W. L. STRAUS, JR.

PREHISTORIC MEN. *Third Edition. Chicago nat. Hist. Mus. Popular Series, Anthropol., No. 37.*

By Robert J. Braidwood; drawings by Susan T. Richert. Chicago Natural History Museum, Chicago. $1.25 (paper). 187 pp.; ill. 1957.

An unusual amount of information about human prehistory is contained in this little book. Frankly intended for the layman, it is written in a deliberately simplified style—at times, almost too simply. At any rate, it is both authoritative and easy to read; hence it should prove to be of particular value in teaching at both the elementary college and the precollege levels.

W. L. STRAUS, JR.

GENETICS AND CYTOLOGY

BIRD HYBRIDS. *A Check-List with Bibliography.* *By Annie P. Gray. Commonwealth Agricultural Bureaux, Farnham Royal, Bucks, England.* 50s. x + 390 pp. 1958.

A review of this volume might be written simply by repeating the title or by repeating the total content. The list of hybrids between species includes those reported in 18 orders of birds, the greatest number of hybrids being reported in the Anseriformes, Galliformes, Columbiformes, Psittociformes, and Passeriformes. Information is given, for each species, of all other species with which it is reported to have hybridized, or with which hybridization has been attempted. The direction of the cross, the sex, and the degree of fertility of the species hybrids have been indicated. Over 1900 reference titles are listed.

M. R. IRWIN

BIOLOGICAL ULTRASTRUCTURE. *By Arne Engström and J. B. Finean. Academic Press, New York.* $8.00. ix + 326 pp.; ill. 1958.

The authors wrote this book to introduce the field of modern biological ultrastructure to a wide variety of students and research workers in the field of the life sciences. In keeping with the introductory nature of the book, citation of the original literature has been kept to a minimum. However, an adequate number of key review articles is cited, so that the reader interested in obtaining further information about a particular field will be able to make an efficient attack on the literature. Although more attention has been paid to zoological than to botanical problems, the authors have succeeded admirably in achieving their stated aims. This book is a good introduction to biological ultrastructure, in that it defines the field, sketches the physical-chemical principles involved, provides examples of current problems, and reports progress in their solution.

Chapter I, From Microscopic Morphology to Molecular Structure, deals with the interrelations between histology and biochemistry. The second chapter, on Methods in Ultrastructure Research, is a discussion of light, electron, and x-ray microscopy, absorption spectroscopy, and x-ray diffraction. The treatment is necessarily condensed. In The Principles of Molecular Structure, which is the third chapter, the electronic theory of valence, the principles of stereochemistry, and molecular interactions are discussed briefly. The fourth through seventh chapters are respectively entitled The Role of Proteins, The Role of Lipids, The Role of Carbohydrates, and The Role of Nucleic Acids. Each of these chapters on biological polymers begins with a physical-chemical description of the monomer, presents the linkage whereby the polymers are formed, and is concluded by a discussion of the incorporation of the polymers into specific cytological structures such as myofibrils, cell membranes, and chromosomes. In the eighth chapter, The Role of Mineral Salts, the structures of calcium carbonate and calcium phosphate are described, and the problem of calcification in tooth and bone tissue is related to these structures. The last chapter, The Role of Ultrastructure in Biology and Medicine, stresses the idea that it is within the basically morphological framework of the structure of living organisms that the dynamic aspects of biological function are confined, and that elucidation of the molecular structure of biological systems defines the framework into which the dynamic activities of biological systems must be fitted.

It is hoped that the results of current and future research will necessitate expansion of this book.

WARNER E. LOVE

GENERAL AND SYSTEMATIC BOTANY

AN INTRODUCTION TO THE PLANT KINGDOM. *By Norman H. Russell. C. V. Mosby Company, St. Louis.* $5.50. 353 pp.; ill. 1958.

In the great flow of new textbooks in botany printed and published in North America in recent years, it is rare to find one which does not require the student to read and work through thick volumes of data of all possible kinds. Russell's book is an exception, and it certainly is no longer than necessary to fit nicely the needs of a short introductory course of the kind most students take at many colleges and universities throughout the continent.

The text is mainly taxonomical and biological, since different biological phenomena of importance are described in a taxonomical order, beginning with the algae and fungi, and continuing up through the mosses and liverworts to the lower and higher vascular plants. Necessary terms are slowly introduced in appropriate places, and good photographs and many drawings of a more variable quality help to explain the phenomena mentioned in the text. Every chapter ends with a short, selected bibliography, and the book itself ends with a comprehensive glossary and a detailed index. The printing is attractive and admirably free from major printing errors, and the binding is as strong as it ought to be for a book of this character.

Although Russell has been able to treat all the major phenomena of common botany in his text, it would perhaps have been wiser and more effective if he had balanced it so that the lower plants were a little less predominant. Also, some of the new and fascinating approaches to modern botany could have increased the stimulatory effect of the book; this

ought to have been easy for the author because of his own experience in studies on the evolution of higher plants. It is doubtful that the author himself really believes in his own statement in the Introduction that "only the method of science is essentially dry and dull." His text contradicts this violently, and so also will his students when they go into the many details filled with his own enthusiasm. The text is to be recommended for introductory courses and also for short courses in botany, especially at colleges and the smaller universities with limited staff and facilities, but it can certainly also be used with success at larger institutions. It will be an excellent help for those teachers who have to prepare a concentrated course in the subject.

ÁSKELL LÖVE

ALGAE. *The Grass of Many Waters. Second Edition.*

By Lewis Hanford Tiffany. Charles C Thomas, Springfield. $6.50. xvi + 199 pp. + 40 pl.; text ill. 1958.

Twenty years have elapsed since the first edition of this brief introduction to the algae was published. The current volume contains a selected assortment of the more interesting and readily understandable facts about the algae, presented expressly for the layman. The emphasis is on the variety found among algae, in form, in color, and in habitat, and these are well illustrated with drawings and photographs. The extremely simplified summaries of the underlying chemistry of growth and the light, whimsical style of writing have the layman reader in mind.

Revision of this edition is slight, except for the insertion of a new chapter, Algae and Research. This discusses the mass culture of algae for food, some recent photosynthesis studies, and the "red tide" problem. It seems a pity that so few topics are included here, when mention could have been made of algae as assay organisms for growth factors or even of their potential use in space travel. Nevertheless, there is no other short and simple book on the algae which includes so many aspects of the subject as this one.

A. COLEMAN

ALGUES DE LA CÔTE ATLANTIQUE MAROCAINE. *La Nature du Maroc, II.*

By Mme. P. Gayral; preface by Pierre Dangeard. Société des sciences naturelles et physiques du Maroc, Rabat. 3,600 fr. iv + 524 pp. + 152 pl.; text ill. 1958.

Contrary to the obvious first guess, this book is not solely a flora of the Moroccan coast. Madame Gayral, a professor at Rabat, hopes to interest both amateur and specialist in the field of marine algae, and for this reason her book includes brief chapters of general information on the systematics, life cycles, elementary marine ecology, and commercial uses of algae. The major portion of the book is devoted to a dichotomous key to the common species, based on vegetative characters, and a subsequent description of each species. These descriptions include simple drawings wherever necessary for clarification of the text, and numerous truly excellent black and white photographs of freshly collected specimens, illustrating more than 150 species.

Although the author includes all genera known from the Atlantic coast area, she purposely omits descriptions of the less common species. She does not include a checklist for the region, nor indicate the extent of her treatment, but an ample bibliography is provided for the specialist. The greatest value of this book lies in its excellent photography of marine algae, indeed some of the best currently available. It might well serve as supplementary material to the usual algal course work.

A. COLEMAN

LIST OF BRITISH VASCULAR PLANTS, *incorporating The London Catalogue of British Plants.*

Prepared by J. E. Dandy for the British Museum (Natural History) and the Botanical Society of the British Isles. British Museum (Natural History), London. 10s. xvi + 176 pp. 1958.

Checklists of the floras of areas otherwise covered with adequate manuals are frequently published in many European countries, and are an invaluable source of correct nomenclature and also of the synonymy of the units they include. Recent lists of this character have been published for the six Nordic countries by Hylander, for Slovenia by Mayer, and for Austria by Janchen, to mention the three most remarkable ones. This year still another such list has been worked out for the British Isles by J. E. Dandy of the British Museum, and its quality is as high as could be expected and its usefulness as great as if it had been a complete flora manual.

During the time when the British flora was covered only by inadequate and old-fashioned manuals, four good checklists were available to those who wanted more reliable information about different aspects of this remarkable flora, namely, the *British Plant List* by Druce, the *London Catalogue of British Plants* by Hanbury, the *List of British Seed-Plants and Ferns* by Britten and Rendle, and the *Checklist of British Vascular Plants* by Clapham. The publication of the most modern flora yet published to cover the British Isles, Clapham, Tutin, and Warburg's *Flora of the British Isles*, might seem to have lessened the need for such a checklist for the time being. The rapid increase in the knowledge of the plants of this area, thanks to the availabiliy of the good manual, and also nomenclatural changes and other necessary alterations have, however, made it desirable that a checklist be worked out before the next edition of the flora can be completed. This new *List of British*

Vascular Plants, which merges into one the old checklists mentioned above, fills this need superbly.

The new checklist begins with a foreword by G. Taylor. The 8 pages of introduction then give a short history of the list and its predecessors before describing the scope of the list and its arrangement. The author neatly avoids informing the reader about the species concept utilized, while he clearly states his adherence to the International Code in selecting the names of species and subspecies, which are the lowest categories included. The introduction ends with an acknowledgment indicating that many of the most outstanding British taxonomists have assisted the author in his difficult task.

The main bulk of the book lists the families, genera, species, and subspecies of vascular plants known to occur in Britain, and their essential synonyms. The arrangement is that of Bentham and Hooker, with some minor alterations, and although the author has taken into consideration recent tendencies in experimental taxonomy, his judgments are moderately conservative. A valuable method of showing the relationships of some recently divided groups is the listing of them under an aggregate species, although this is not, and cannot be, done consistently and is sometimes directly misleading.

There may be a few misprints here and there in the list, and the consistency in the species concept is as variable as with most other authors. Some readers may find that the author has been unduly conservative in keeping names which are obsolete, whereas others may just as easily make remarks on the replacement of old and established names with others unknown to most botanists. Such remarks cannot be avoided, since nobody is ever able to follow all the good counsel of everybody else. The fact remains, however, that Dandy has, in most cases, been able to sail securely between the skerries of changing nomenclature, and his judgment has been wise in most of the critical cases he lists.

A detailed description of the list is not possible, and an exact discussion of its content is out of place here. It must be pointed out, however, that this is one of the very best checklists available, and every botanist with interest in European plants or European weeds abroad will here find a reasonable solution of many problems in nomenclature. The English botanists in general, and Dandy in particular, have reason to be proud of this excellent achievement.

ÁSKELL LÖVE

PLANT MORPHOLOGY AND DEVELOPMENT

ORIGIN OF PRIMARY EXTRAXYLARY STEM FIBERS IN DICOTYLEDONS. *Univ. Calif. Publ. Bot., Vol., 30, No. 2.*

By Amélie Blyth. University of California Press, Berkeley and Los Angeles. $1.75 (paper). iv + pp. 145–183 + 23 pl. 1958.

PLANT PHYSIOLOGY

METHODEN ZUR BESTIMMUNG PFLANZLICHER WUCHSSTOFFE.

By H. Linser and O. Kiermayer. Springer-Verlag, Berlin. $7.85. vii + 181 pp.; ill. 1957.

This book presents a summary of most of the published methods for the extraction and assay of natural and synthetic auxins.

It has often been observed that it is difficult to compile inclusively and at the same time to evaluate. Completeness and balance, in other words, seem often mutually exclusive. The authors' zeal in including an account of all the odd and little-known methods results in the presentation of some of these almost as fully and prominently—although they may have only once been described and never used—as methods, like the *Avena* curvature test or the coleoptile straight growth test, which have been widely and internationally used for years. Another curious feature of the book is that the calibration curves for the various bioassays are presented as response plotted against the logarithm of the auxin concentration (in percentages!). Those tests which are effective only over a narrow range, or those in which the proportionality between response and concentration is linear, thus give only fragmentary curves which to the inexperienced eye might make them look useless; on the other hand, tests like Linser's own, in which the auxin is dissolved in lanoline and applied unilaterally to *Avena* coleoptiles, show a relatively wide range of effective concentrations, although the response is neither linear nor log-linear over any appreciable range. This latter test, although not often used outside the author's own laboratory, is presented in the greatest detail, with response curves of many different substances, tables of results, and mathematical analysis.

Another difficulty is that the usefulness of the various procedures is not compared. A brief "Kritik" of each method is given, but this is often only a few words, and a newcomer to the field would find little guidance as to the method of choice for his own problem. He might find the book a useful index to the literature, however, though even here there would be a limitation, not only because the methods are often summarized too briefly for direct laboratory use, so as to make a check with the original literature unavoidable, but also for the following, more fundamental, reason. This is that the authors have, perhaps understandably, concentrated their attention on European contributions, with the result that the voluminous American literature of recent years, as well as that from Japan, is mainly omitted. Although

the Preface is dated March 1957, I could find references only to 9 American papers later than 1952. In consequence, much of the chromatographic work, the abscission test, and all the work with C^{14}-labeled indoleacetic acid are omitted. Even for the period before 1952, the coverage of the American literature is very uneven. These omissions must lessen the value of the book to readers in both continents.

In casual reading several misstatements were noted, such as that KCl *reduces* the growth of coleoptile sections (p. 110) or that the pea curvature test shows extraordinary sensitivity to metals (p. 72). It is to be hoped that a more careful study would not reveal too many more. Typographical errors are, of course, inevitable, and this book is no exception.

It is easy to criticize, of course, and hard to synthesize. The authors deserve commendation for the good idea of bringing all this scattered material together into one place, and for the useful job of assemblage they have done. The book is well printed and produced. The price is rather high.

KENNETH V. THIMANN

ECONOMIC BOTANY

THE MANGO.

By S. R. Gangolly, Ranjit Singh, S. L. Katyal, and Daljit Singh; foreword by Ajit Prasad Jain. Indian Council of Agricultural Research, New Delhi. $12.00. xiv + 530 pp. + 228 pl. 1957.

The mango is one of those tropical fruits northerners dream about, and it has long been known as the most praiseworthy of the many kinds of delicate fruits the peoples of the tropics, and of India in particular, enjoy daily. The flavor of the fruit is said to be indescribable; its taste can be compared to nothing else. The plant has been cultivated in southern Asia from time immemorial, and it is referred to in the most ancient scripts. The poets of the past have mentioned the mango in their poems more frequently than other food, and the sculptors have immortalized it on rock. In addition to its beauty, this fruit is a valuable source of food for hundreds of millions of people, and others also would like to be able to enjoy it far from its original area.

As might be expected of a plant cultivated for so long a time, there is such an infinite variety of mangoes in India that a systematic description and listing of the varieties, with information on their botanical peculiarities, has been a long-felt need. The Indian Council of Agricultural Research has now made an earnest attempt to fill this need, and there can be no doubt that the present treatise will be of paramount importance to grower as well as consumer. Also, it is an excellent reference work for those interested in scientific studies of the mango and its breeding in India and elsewhere.

The first part of the book deals with the origin, history, uses, and botany of the mango. There is a description of 210 varieties, which all seem to belong to a single species, *Mangifera indica*. The varietal descriptions are based on the nature of the terminal panicles, shape, color, flavor, and taste of the fruit, position of the leaves on the stem, nature of the folding of the leaves, etc. All these and other characteristics seem to be of great diagnostic value. Added to a detailed description of each variety is a color plate of the fruit, so that even a layman will have no difficulty in identifying his own plants and fruits among the varieties here named. These plates are of such a high quality that they can be compared with the very best pictures published of other fruits elsewhere, and one can almost feel their differences in flavor and taste by looking at the attractive pictures! It is pointed out that while several of the varieties are regarded as the very best for the table, others are better fitted for pickles and chutneys, a classification of great value for those who may visit India or want to introduce any of these varieties into other regions.

The same variety is sometimes known by different names in different parts of the country, and the nurserymen are unable to label them properly. This fact may have discouraged those who wished to introduce the mango into their own countries. The present book should be of immense assistance to such persons, and it will most probably be used very frequently outside India just because it eliminates such difficulties in naming the varieties. The book also lists the quality of the fruit, its susceptibility to diseases, its keeping and packing qualities, and other information of great significance. Since the plant needs many years before it starts to yield fruit, one must know the variety to be selected at the time of planting, and a poor choice will be an expensive experience discoverable only after many years.

The latter part of the book deals with the culture of the mango. Here methods of cultivation are discussed, and also the various pests and diseases which may destroy the fruit at different times during its growth. An understanding of early-bearing, mid-season, and off-season varieties is necessary to secure a fairly continuous market, and the book gives details concerning selection and treatment in different parts of the country to achieve this goal. In addition, a rather technical section discusses the cultivation and propagation of the plant, how to raise it from seedlings or from buds of different kinds, and various methods of helping the plant to give as much fruit as possible in different climates.

There can be no doubt that this fine book about the mango is of the highest quality and of the greatest importance to fruit growers everywhere in the warm regions where this plant is able to thrive. It ought to be placed in all libraries of fruit growers in southern areas and also in botanical libraries

where research workers will thereby be enabled to get reliable information about this most delicate of all tropical fruits.

M. S. Chennaveeraiah & Áskell Löve

GENERAL AND SYSTEMATIC ZOOLOGY

Grundriss der allgemeinen Zoologie. *Thirteenth Edition.*

By Alfred Kühn. Georg Thieme Verlag, Stuttgart. $4.25. viii + 289 pp.; ill. 1959.

This thirteenth edition of Kühn's *Grundriss der allgemeine Zoologie* represents the latest revision of what has now become a classic in the German speaking world. As the reader will notice, it has received frequent revision, an indication of its general popularity. It is a short, complete text covering concisely, almost in outline form, the traditional material of a general zoology course. Actually, this is a companion to the *Zoologische Praktikum* which has no counterpart in the English-speaking world. To an English-speaking person who reads German with any facility, this would represent a really excellent reference work to general information about zoology. The topics covered include: the general properties of life, the body plans of animals (a phylogenetic consideration), a brief consideration of animal physiology, genetics, embryology, and ecology. Evolution is also presented in a very brief section.

Ronald R. Cowden

Sea Shells of Tropical West America. *Marine Mollusks from Lower California to Colombia.*

By A. Myra Keen. Stanford University Press, Stanford. $12.50. xii + 624 pp. + 10 pl.; text ill. 1958.

This work deals with the fauna of an area of the Pacific Coast extending southward from Cape Abreojas to Panama. The well-written descriptions, together with the plates, some of which are beautifully colored, and some of which depict species that have been previously unfigured, make the identification of more than a thousand species a relatively simple matter.

From the time when Padre Eusebio Francisco Kino gathered on this coast the first shells of which we have any historical record, to the time when the late Herbert N. Lowe made his extensive collection, now the property of the San Diego Society of Natural History, this area has been a terra incognita to collectors. Many of the medical personnel who accompanied expeditions of a political or commerical nature gathered material in Pacific American waters. Such collections eventually made their way into the leading museums of this country and Europe, but these efforts were little more than desultory. Today, however, conditions have changed. The devastation of Europe by two world wars has to a large extent diverted tourist traffic to Latin America, and the sleepy coastal villages of Mexico and Central America are becoming tourist-conscious and are actively catering to this influx of visitors. As many of these persons are conchologists, a steady stream of material has been flowing into the museums of the United States, bringing nondescript species and varieties for which new names are needed. Also expeditions from many institutions of learning enter the same territory year by year, so that the number of new species is increasing, as well as the number of species which are now being recognized as identical with still older species. In addition, the larger series of older species which are accruing make it possible to revise their systematic positions with greater accuracy. The result is a condition of temporary confusion which this book will help to dispel. Its appearance is most timely, and the care which has gone into its production, not only by the author but also by the proof-reader, makes it a valuable contribution to West Coast conchology. It will be found equally helpful both to the beginner, who will be delighted with its illustrations, and to the advanced student, who will be delighted with its extensive bibliography.

Joshua L. Baily, Jr.

Checklist of the Millipeds of North America. *U. S. Nat. Mus. Bull. 212.*

By Ralph V. Chamberlin and Richard L. Hoffman. Smithsonian Institution, Washington, D. C. $1.00 (paper). iv + 236 pp. 1958.

There is a real need for this checklist, for the scattered nature of the literature on the millipeds of North America has been such a deterrent to their study that only a few biologists are aware of the great range of forms within this interesting class of arthropods. Millipeds as short as 3 mm. and as long as about 170 mm. are known from the United States. The fewest body segments is 11 and the most is nearly 200. There is a variety of brilliant body color combinations in addition to the more common brown. The odor of the repugnatorial secretions is varied and sometimes very startling and pleasing. The habitats include caves, deserts, and newly formed marine islands in addition to pastures, gardens, and woodlands from Alaska to Key West.

Biologists who lump millipeds into categories such as "fontaria," "julus," "spirobolus," and "polydesmus" will find some surprises when they consult this checklist. The genus *Fontaria*, for example, is now restricted to 2 species in Georgia and South Carolina, and the representatives of the many other fontaria-like groups within our borders are distributed among some 39 other genera. In all, Chamberlin and Hoffman have recorded 749 species and subspecies, which fall into 200 genera, 35 families, and 11 orders. They call attention to the fact that in

most cases groups have been recorded as they were published and that almost all groups are in need of much more collection and careful evaluation. Doubtless many new forms are yet to be described, particularly from the Western States. There are problems enough to keep many serious students occupied for many years.

Keys to orders and families are included. Unfortunately, there are some errors in these keys: the Cyclodesmidae do not have repugnatorial pores; some members of the Paraiulidae have the anterior and posterior gonopods very unequal in size and the posterior pair concealed; and some members of the Polyzoniidae do have hairs on the dorsum.

NELL B. CAUSEY

ANNUAL REVIEW OF ENTOMOLOGY. *Volume 3.*

Edited by Edward A. Steinhaus and Ray F. Smith. Annual Reviews, Palo Alto. $7.00. viii + 520 pp.; ill. 1958.

The entomological literature up to the middle of 1957, is covered in this volume. As in earlier volumes of the series, there is still one needless deficit; many of the reference lists are illogically arranged, in order of citation. Also, as in the two earlier volumes, there is a preponderance of articles on insect control: Clausen, on biological control; Popham and Hall, on insect eradication programs; March, on acaricides; David, on organic phosphorus insecticides; Fay and Kilpatrick, on insecticides for adult Diptera; Gyrisco, on forage insects; and Balch, on forest insects. The number of these articles (while reflecting the number of publications on these topics) bears little relation to the generality of interest in the subject of control. It seems that there are numerous, more appropriate periodicals in which to place such extensive reviews. More desirable, it seems to me, are the several articles which cover areas of research in which insects are merely happy choices of experimental animals for use in the study of general biological problems, or in which they are atypical. Roeder and Hodgson review two active areas of research, the nervous system and chemoreception, respectively. Richards and Brooks critically and thoughtfully appraise the unique internal symbiosis in insects. Frings and Frings summarize sound production and perception. Population dynamics is again reviewed by Nicholson in a debate which naturally centers about the involvement of density-dependent control. A nicely integrated treatment of honeybee genetics and breeding is provided by Rothenbuhler. Friend summarily covers the important subject of feeding of phytophagous insects, and Painter examines plant resistance to insects. The remaining chapters treat the subjects: silkworm nutrition (Legay); ovarian development, structure and vitellogenesis (Bonhag); phylogeny of the panorpoid orders (Hinton); zoogeography (Gressitt); hybridization and speciation in mosquitoes (Rozeboom); feeding behavior of biting flies (Downes); biology of the Scarabaeidae (Ritcher); and the transmission of plant viruses by insects (K. M. Smith).

D. R. EVANS

PALMER'S FIELDBOOK OF MAMMALS. *A Unit in a Series of Aids to Conservation.*

By E. Laurence Palmer. E. P. Dutton & Company, New York. $3.75. 321 pp.; ill. 1957.

Palmer's book is one more in a growing list of handbooks on mammals. Its general organization is not remarkably different from that of others which have appeared recently, approximately one page being devoted to each species. At the top of the page is a pen sketch of the animal and usually a sketch of the skull, droppings, or tracks as well. Less frequently, other parts of the skeleton may be featured. A condensed account of the life history, structural features, and economics of the species appear below.

While the American fauna is emphasized, selected species from elsewhere are included. Thus one will encounter the hedgehog along with the American shrews and moles, the hamster along with other cricetines, etc., as well as lions, tigers, giraffes, and other mammals commonly seen in zoos. No less than 101 pages are devoted to the domestic breeds of mammals. In addition, there are the usual introductory pages concerning mammalian characteristics, their special senses, reproduction, etc.

It is somewhat of a shock to find on the inside front cover a "family tree" in which the relatively trivial divisions of Cenozoic time are blithely equated with the major time divisions of Mesozoic and upper Paleozoic. The book may prove handy for city folk, but it is hardly the fieldbook that its name implies. One gets an impression that it is really aimed at the urbanite, whose experiences with mammals are expected to be confined largely to domestic kinds and those to be seen in zoological gardens.

BRYAN P. GLASS

LES SCORPAENIDÉS DES EAUX MAROCAINES. *Trav. Inst. Sci. Cherifien, Sér. Zool., No. 15.*

By Henri Boutière. Société des Sciences Naturelles et Physiques du Maroc. 1,000 fr. (paper). 83 pp. + 5 pl.; text ill. 1958.

THE MAMMALS OF BANKS ISLAND. *Arctic, Technical Paper, No. 2.*

By T. H. Manning and A. H. Macpherson. The Arctic Institute of North America, Montreal. $1.00 to members of the Institute; $2.00 to nonmembers; (paper). 74 pp.; ill. 1958.

ECONOMIC ZOOLOGY

LIVING RESOURCES OF THE SEA. *Opportunities for Research and Expansion.*

By Lionel A. Walford. The Ronald Press Company, New York. $6.00. xviii + 321 pp.; ill. 1958.

Every thinking fishery biologist, especially if he occupies a position of administrative responsibility, sooner or later begins to worry about the value of his accomplishments. A universal fishery problem is variation in supply, in catch, or in price, and a major purpose of fishery science is to delineate, to explain, and to recommend measures for minimizing such variations. The biologist is in an unenviable position, knowing that he is operating with insufficient knowledge and suspecting that he is progressing toward his objective less rapidly than the march of the many factors that are operating to change the characteristics of the resources he is trying to maintain.

The marine fishery biologist, particularly, is working in a medium so vast and with resources so puny that he can hardly be blamed if he succumbs occasionally to moments of despair. Even though his accomplishments still fall far short of their goal, he is already overwhelmed by a literature so immense and diffuse that he cannot attend to his everyday work and keep up with significant developments in his field of interest. In no other branch of science must a competent worker understand so many disciplines —mathematics, physics, chemistry, geology, geography, engineering, economics, sociology, and all the major branches of biology. It is only recently that attempts have been made to summarize the principles and accomplishments of fishery science in comprehensive fashion. By far the best effort to date has been the British work *Sea Fisheries*, edited by Michael Graham; but even this outstanding work gives only passing attention to the great gaps in our knowledge that prevent application of the rather clear-cut principles of fishery management. Many a reader of Graham's book might adopt a complacent view of the accomplishments of fishery science in its approximately 75 years of existence as a distinct branch of science.

Such readers would certainly be shaken out of their complacency by Walford's book, which in many ways serves as a fitting complement to the contribution of Michael Graham and his collaborators. As Fairfield Osborn has observed so truthfully in the the Foreword: "Its author, with restless purpose, seeks to demonstrate not so much what is known as what is *not known*." Walford is eminently qualified to speak on his chosen subject, for he has held positions of importance in American fishery research for many years, including a long and productive term as Chief of the Branch of Fishery Biology of the United States Fish and Wildlife Service. He is well known internationally as an inquiring and independent thinker who has little patience with complacency and the conventional approach.

The book is divided into two parts: The Marine Wilderness, and The Resources of the Sea. The first expounds the question that led to the study: "What scientific researches, apart from those which are in progress, would contribute significantly toward learning how to enlarge the yield of food from the sea in answer to human needs?" and enlarges upon three assumptions that underlie it: "(1) We have not yet learned how to exploit the food resources of the sea fully; (2) scientific research will show the way; (3) there are gaps in present research programs which need filling."

The 12 chapters in Part I exhibit a certain unevenness in quality and thoroughness of treatment, as might be expected in treating so vast a subject, which ranges from geography to the improvement of vessels and gear. Chapter 3, entitled Conservation, seems somewhat unsatisfactory. It is a curious mixture of the simple and the complex, perhaps purposely so, but the advantages of such treatment are not clear. The last sentence of the introduction raises hope that constructive and novel steps toward better scientific management will be proposed, but this expectation is not clearly fulfilled. The author does make the telling point that governments, while they are the proper agencies to conduct fishery research, have been confined by limited budgets to the more valuable commercial species, and that the universities have not fully accepted the challenge to develop the philosophical aspects. Chapters 4 and 5 are thoroughly stimulating, the first an eloquent appeal for greater attention to taxonomic problems, the second a fairly comprehensive discussion of the need for a better understanding of environmental relationships.

Part 2, consisting of 5 chapters, reviews some gaps in our knowledge of economically valuable marine plants and animals and suggests ways in which this knowledge can be improved. Some rather surprising deficiencies appear, e.g., here, as elsewhere in the book, shellfish resources are given brief and rather incomplete attention, not commensurate with their present and potential importance.

The final chapter, Looking Forward, summarizes the status of present knowledge and demonstrates clearly that few final answers have been obtained, and few are in sight. The author believes that marine research is not adequately staffed or financed, and that if we wish to exploit the sea to full advantage, we had better increase our investment and effort.

The reader who is looking for clear-cut answers to the mysteries of the sea will not find them in this book, for it is obvious that this was not the author's intent. What he will find is an unusual approach to the question of exploitation and management of

marine resources, with statements of many stimulating problems that cry for attention. Students will gain perspective and insight vicariously from the author's long experience with marine research, and his colleagues will recognize many parallels with their own thinking, which may stimulate them to further inquiry.

Technically, the publisher has produced a book that is generally pleasing in appearance, but the contrast between light buff paper for text and dead white for illustrations is unfortunate, though perhaps necessary. The charts, a useful feature of the book, have been placed carefully between chapters as far as possible, so that they do not interrupt the train of thought. Particularly commendable are the comprehensive legends, a feature that could well be adopted by other authors.

Eleven pages of notes and references, and 13 pages of index increase the value of this book as a work of reference.

J. L. McHugh

LIVING SILVER.

By Burns Singer; illustrated by Robert Frame. Houghton Mifflin Company, Boston. $3.75. viii + 232 pp.; ill. 1958.

This is a curious but interesting book, described by the anonymous bard of the dust jacket as "a remarkable fusion of science, adventure and quiet philosophy." It has as a central character an exiled Pole who learns to love the sea, and in the end we find that he is off for Glasgow to study fisheries biology in the University. For the most part, the book concerns fish and commercial fishing and ought to be considered essentially a popularization of those subjects. Since there is no plot or character development, the book cannot be considered a novel. It is nevertheless a very well-written account of the biological and fisheries aspects of the fish around Scotland, and something like it about our own fisheries would be a most useful contribution to public understanding.

Joel W. Hedgpeth

ANIMAL GROWTH AND DEVELOPMENT

MORPHOGENESIS: THE ANALYSIS OF MOLLUSCAN DEVELOPMENT.

By Chr. P. Raven. Pergamon Press, New York, London, Paris, and Los Angeles. $10.00. xii + 311 pp. + 12 pl.; text ill. 1958.

This is an attempt to record everything definitely known about molluscan development in a single book. It is strictly a compendium of facts upon which the reader may theorize and from which he may draw his own conclusions. The author makes no suggestions as to how the facts which he records should be interpreted.

As an example of the author's procedure, we may note the careful way in which he describes in detail the process by which the original bilateral symmetry of the more primitive Gastropoda has been lost, and those by which a secondary bilateral symmetry has been partially regained by the more specialized members of this class. More than a dozen different explanations of the first process have been offered by different students of this group, the causative factors of which are listed, but no comparative judgments are rendered here because these explanations are so far only in a theoretical stage, and the author is interested only in facts. The second process, by which the bilateral symmetry has been partly restored, is apparently a more complex one, and fewer explanations have been offered to account for it. It has been suggested that the processes in the Pulmonata and the Opisthobranchiata, although they lead to the same result, are fundamentally different, so that these two groups are not nearly so closely related as they have been supposed to be by some past writers. Again the author describes carefully the parallel processes in the two groups, but makes no effort to interpret the differences between them.

Every attempt to construct a taxonomic system for the Mollusca has been based upon the modifications of structures whose evolution has been in the direction of simplification, so that undue importance has been laid upon similarities between forms which resemble each other only because they have lost the features by which their progenitors could be distinguished. The importance to the systematic malacologist of an understanding of the evolutionary changes through which species have passed, as recorded in their ontogenetic development, is obvious. But it is still too soon to theorize, because we do not yet have enough facts. The generally accepted division of the scientific method into three stages—the acquisition of facts by experiment and observation, the classification of facts and their interpretation, and the formulation of laws of nature by drawing inferences from these facts—is theoretically sound, but systematic malacology has not yet gotten out of the first stage, and those students who feel the need of a better knowledge of the facts can do no better than to read, mark, learn, and inwardly digest the contents of this book.

An interesting feature of this work is that in the introductory chapter about six genera are referred to by names which the International Commission on Zoological Nomenclature has declared to be invalid. No disparagement to the author is intended. It would be quite unreasonable to demand from an author of such a work as this that he waste his time acquiring a knowledge of the complexities which the Commission is continually adding to the Code. The

matter is mentioned only to give prominence to the result that inevitably must occur whenever the rules of nomenclature in any science are entrusted to orismologists rather than to those who will actually use the nomenclature—the scientists themselves. Perhaps no better argument could be advanced in favor of a saner nomenclatorial policy than this book, so worthy of the highest praise.

JOSHUA L. BAILY, JR.

THE BIOLOGY OF HAIR GROWTH.

Edited by William Montagna and Richard A. Ellis. Academic Press, New York. $15.00. xviii + 520 pp.; ill. 1958.

The hair follicle is a kind of "biological microcosm" in which almost any problem relating to growth, differentiation, decline, and rejuvenescence of tissues can be studied to advantage. In the present volume, which is the outgrowth of a conference sponsored by the British Society for Research on Ageing and held at the Royal College of Surgeons in August, 1957, 23 contributors from Britain, the United States, Japan, and Germany provide 21 chapters aimed at presenting a comprehensive view of the development and function of hair follicles and related structures. The book is in no sense a historical treatise, but the authors have been fairly successful in skimming the cream from earlier publications and integrating it with the less concentrated products of current research. The emphasis on recent work—and perhaps an index of the rate at which new publications are appearing—is revealed by the fact that of some 900 bibliographic references about 60 per cent cite articles that have been published since a somewhat similar conference on hair was held at the New York Academy of Sciences only eight years ago.

Most of the discussion is based on human material, although data from the rat, and to a lesser extent from the sheep and some other mammals, contribute to the over-all picture. Some of the still unexcelled figures from Stöhr (1903) are again reproduced, while new models made of balsa wood serve to illustrate, as nothing else can, the general topography of pilosebaceous units. Numerous photomicrographs, which vary from very good to less than excellent, are supplemented by an abundance of lucid and informative diagrams, some of which will probably find their way into future textbooks. The anatomy and function of the follicle is presented in terms of the best available information. There is a detailed discussion of histochemical changes in its layer during development, the biosynthesis of fibers, the chemistry and the electron microscopy of keratinizing tissues, and a consideration of such matters as nutritional and hormonal effects, and the influence of age, sex, and genetic constitution upon hair as seen in American and Japanese populations. With reference to biochemical and ultramicroscopic aspects of the developing hair follicle, one is perhaps justified in the inference that the subject is well launched in its descriptive phases but has not quite reached the stage for adequate syntheses.

An especially provocative chapter deals with the still moot question of the neogenesis of hair follicles in the adult skin. It is commonly assumed that this does not occur, even after transplantation or in wound healing, but the evidence is inconclusive, and one striking example is cited to show that it can happen, and regularly does so, in the velvet of the deer's antler which is regenerated de novo every year.

One other matter of especial interest may be noted briefly. Since the stimulating work of Rawles a few years back, the mechanisms involved in the origin and dispersal of granular pigments have received renewed attention, and we are now told that it is the cells of the hair which phagocytose granules in melanocyte processes—a complete reversal of views expressed half a century ago by Metchnikoff, who possibly observed the phenomenon but read the evidence backward.

Various other aspects of the subject which the student of hair might wish to see treated could have been included, but as it stands the volume is a valuable compendium which will probably serve as a standard reference work for many years to come.

C. H. DANFORTH

ANIMAL MORPHOLOGY

ELECTRON MICROSCOPIC ATLAS OF NORMAL AND LEUKEMIC HUMAN BLOOD.

By Frank N. Low and James A. Freeman. McGraw-Hill Book Company, New York. $25.00. x + 347 pp. 1958.

From looking at the beautiful electron micrographs in this book, one could almost build a course on the electron microscopic morphology of the animal cell. In this particular respect it should be of interest to the biologist. Especially beautiful, if any single thing must be cited, are the 70,000–80,000 × pictures of the eosinophilic granules showing their areas of differing density. From this atlas it may also be seen that by using the electron microscope the differences may be resolved between the structure of cell types which appear similar in light microscopy: plasma cells can be distinguished from the lymphocytes by virtue of the exaggerated endoplasmic reticulum of the former. From a biologist's point of view, the pathological cells shown are of interest in that they demonstrate some of the secondary changes that occur in the various leukemic cells. In every sense of the word this is an atlas. The types of cells and the various classes of cellular inclusions have been presented in considerable detail. The text is limited

to a brief introduction to the general subject of each section, an explanation of the plates, and the pertinent references.

R. R. Cowden

Primatologia. *Handbook of Primatology. Verdauungstrakt—Urogenitalorgane—Endokrine Organe. Volume III, Part 1.*

Edited by H. Hofer, A. H. Schultz, and D. Starck. S. Karger, New York and Basel. S.Fr. 188.50; $47.00. xviii + 824 pp.; ill. 1958.

This volume, one of a series of handbooks on the comparative gross and microscopic anatomy of non-human primates, is divided into 3 main parts concerned with the digestive tract, the urogenital system, and the endocrine organs, respectively. Each main part is in turn divided into sections and chapters, written by different individuals, in which the comparative gross and microscopic anatomy of the various organs are systematically described for the different primate genera. Each chapter is well illustrated and includes an extensive bibliography of references from the 17th and 18th centuries to some as recent as 1956.

Part I (Digestive System) is subdivided into 2 sections, one on the oral cavity and vestibule and the other on the pharynx, esophagus, stomach, intestine, and liver. The first section consists of a chapter on the vestibule of the mouth and the morphology of the salivary glands by R. Schneider (Frankfurt am Main), a chapter on the microscopic anatomy of the salivary glands and the exocrine part of the pancreas by W. Burkl (Wien), a chapter on the tongue and soft palate by R. Schneider, and one on the palatine ridges by A. H. Schultz (Zürich). The second section is composed of a chapter on the gross form and position of the pharynx, esophagus, stomach, and intestines by W. C. O. Hill (London), a chapter on the microscopic anatomy of the esophagus, stomach, and intestines by W. Burkl, a chapter on the anal region, chiefly histology, by R. Ortmann (Frankfurt am Main), a chapter on the form, gross anatomy, internal anatomy, and histomorphology of the liver, gall bladder, and bile ducts by W. Lipp (Graz), and a chapter on the abdominal cavity and topography of the abdominal organs by D. Starck (Frankfurt am Main).

Part II (Urogenital Organs) is subdivided into a section on the urinary system by W. L. Straus, Jr. and J. R. Acadi (Baltimore) and one on the reproductive system. The latter consists of a chapter on the internal reproductive organs written by P. Eckstein (Birmingham) and a second on the external genitalia written by W. C. O. Hill.

Part III (Endocrine Organs) consists of a chapter on the hypophysis written by B. Hanström (Lund), one on the suprarenal gland by R. Bachmann (Göttingen), one on the thyroid and parathyroid glands by W. Bargmann (Kiel), another on the thymus by the same author, and a final chapter on the islands of Langerhans by A. Thiel (Kiel).

Those interested in quantitative data will find tables on averages and the range of variations in the type and extent of palatal ridge patterns; the distribution of the number of palatal ridges in chimpanzees and whites; the variations in number of palatal ridges in different human groups; the occurrence of striated muscle in the esophagus of men, apes, monkeys, and lemurs; the presence and distribution of cells of Paneth in different parts of the intestine of lemurs and monkeys; the distance between the ano-rectal and the ano-cutaneous lines as well as other histological features of the anal canal of non-human primates; variations in the external form of the primate liver; the relative length of the various parts of the primate intestine; the relative weight of the primate kidney in the newborn and adult; the distribution of the 5 types of renal medulla in various primate genera; the number of renal corpuscles/mm² in different primates; the mean, standard error, and range of variation in renal corpuscle diameter and estimated percentage of area occupied by renal corpuscles in various primate kidneys; the dimensions of the ovary; the size of the non-gravid uterus; and the proportionate size of the suprarenal glands.

The system of classification, prepared by W. Fiedler (Frankfurt am Main), followed in the book is presented in tabular form at the beginning. Two suborders, Prosimiae and Simiae, are recognized. The latter corresponds to suborder Anthropoidea in Simpson's 1945 classification of mammals. The Prosimiae consists of two superfamilies: Tupaiiformes, composed of the Anagalidae and the Tupaiidae; and Lemuriformes, composed of the Lemuridae, Inriidae, and Daubentoniidae. The suborder Simiae consists of two infraorders: Platyrrhina (New World marmosets and monkeys) and the Catarrhina (Old World monkeys, apes, and man).

The sections of the book on the palatine ridges, the form and position of the pharynx, esophagus, stomach, and intestine, and the urogenital organs are written in English. The rest of the book is in German. This is a valuable reference book for all students of the comparative gross and microscopic anatomy of primates.

F. G. Evans

ANIMAL PHYSIOLOGY

Annual Review of Physiology. *Volume 20.*

Victor E. Hall, editor; Frederick A. Fuhrman, and Arthur C. Giese, associate editors. Annual Reviews, Palo Alto. $7.00. viii + 633 pp. + 1 pl. 1958.

One of the more valuable aids to the researcher in this age of prolific scientific publishing is a good critical "review." In its twentieth year, the *Annual Review of Physiology* appears to have changed little in its form and extent of coverage. But the editors point out that the estimated number of papers to be reviewed has almost doubled, a fact suggesting that the number of papers covered has been considerably restricted. This may in part be compensated by more succinct reviewing but, according to the editors, the coverage is less complete than in earlier editions.

Whether restricted coverage is commensurate with good reviewing is conjectural. A review such as this series should not be a complete abstracting service but rather a survey of the significant contributions within a particular area, however broad or restricted it may be. To me it seems that the reviewers have, in general, done remarkably well in this respect.

With the exception of an interesting prefatory chapter on the study of some fundamental problems in aquatic organisms, by W. J. V. Osterhout, and of a review of comparative physiology of excretion, originating this year, this volume does not stand out in any particular way from others of recent years. The subjects selected include studies on animal mitochondria, hormonal regulation of growth, physiology of muscle, heart, respiration, digestion, and vision. The interrelationships of hypothalamus, adenohypophysis, and adrenal cortex have been reviewed, and 3 other separate reviews cover the somatic, visceral, and cerebral functions of the nervous system and the pharmacological aspects of central and synaptic transmission. Peripheral circulation has been considered from the pharmacological aspect, the kidney from the point of water and electrolytic metabolism; in blood, work on the formed elements has been reviewed. In keeping with recent policy, some phase of Russian physiology is also examined, the subject chosen for this volume being cardiovascular physiology, dating back to 1952. In all respects, Volume 20 maintains the high standards of the predecessors.

THOMAS E. NELSON, JR.

LIVER-BRAIN RELATIONSHIPS.

By Ian A. Brown. Charles C Thomas, Springfield, Ill. $6.50. xiii + 198 pp. 1957.

In the words of the author, "This monograph is but a discussion of the relationships that exist between the organs and no pretense is made to solve the problem." Brown originally prepared the material as a thesis, and it is more than sufficiently documented with over 400 references. The author's own original contribution to the study consists of a clinical and pathological analysis of 82 patients with hepatic disease, 42 of whom progressed to a state of hepatic coma and died.

The monograph is a creditable review of the many suggestive correlations existing between two extremely complex and poorly understood organs. Considered, however, from the standpoint of directed original research and as a thesis presented for a graduate degree in medicine, it demonstrates an all-too-prevalent tendency to permit graduate students to take on problems which, by their herculean proportions, promise little reward short of a lifetime of study.

THOMAS E. NELSON, JR.

SHOCK AND CIRCULATORY HOMEOSTASIS. *Transactions of the Fifth Conference, November 30, December 1 and 2, 1955.*

Edited by Harold Green. Josiah Macy Jr. Foundation, New York. $4.75. 337 pp; ill. 1957.

This is the last of five conferences on shock and circulatory homeostasis. The communications in this volume are concerned with Hepatic Blood Flow in Experimental Shock (Stanley E. Bradley); The Bacterial Factor in Experimental Shock (Jacob Fine); An Inquiry into the Mechanism of the Protection Afforded by Aureomycin Against Shock (Silvio Baez); Shock in Germ-Free Rats (Benjamin W. Zweifach); Influence of Adrenergic, Cholinergic, and Ganglionic Blocking Agents in Experimental Shock (Silvio Baez); Humoral Factors in Experimental Shock (Benjamin W. Zweifach); Preservation of the Hepatic Ferritin Systems and Protection Against Shock by N-(2-chloroethyl)-N-(cyclohexylmethyl)-ethylamine hydrochloride (G-D 131) (Ephraim Shorr); Influence of Hypothermia: Chlorpromazine (Michael E. DeBakey); and Lymphatic Adjustments in Shock (Silvio Baez).

The format and editing of this volume are up to the usual high standards of Macy Conference Transactions. As in the previous 4 volumes, the provocative discussions by prominent investigators are recorded. Publication of the entire informal proceedings, of course, has many advantages, but the reader frequently feels that the discussions are getting nowhere. A summation of salient points of each presentation would be a valuable addition. Nevertheless, the discussions are, in general, highly stimulating and provide clinicians and physiologists with thought regarding future research.

SHERWOOD M. REICHARD

RECENT PROGRESS IN HORMONE RESEARCH. *Proceedings of the Laurentian Hormone Conference 1957, Vol. XIV.*

Edited by Gregory Pincus. Academic Press, New York and London. $13.50. viii + 582 pp.; ill. 1958.

The 14 papers presented in this volume represent some of the diverse approaches to five major areas of contemporary endocrinologic research.

Section I discusses Hormonal Structure and Function. It includes 4 papers: The Chemistry and Biological Activities of 16-Hydroxylated Steroids (Bernstein); Structural and Hormonal Activity of Some New Steroids (Drill and Riegel); Molecular Structure of Steroids and Phenanthrene Derivatives Related to Growth of Transplanted Mammary Tumors (Huggins, Mainzer, and Briziarelli); Studies on the Mechanism of Action of Estrogens (Mueller, Herranen, and Jervell). Section II is devoted to Hormones in Growth and Development. The 3 papers in this section are Hormones and Protein Nutrition (Leathem); Effects of Hormones on Growth, Fattening, and Meat Production Potential of Livestock (Gassner, Reifenstein, Algeo, and Mattox); and The Hormonal Control of Mammary Growth and Lactation (Lyons, Li, and Johnson). Section III deals with two Aspects of Reproduction: Cytologic Tests of Chromosomal Sex in Relation to Sexual Anomalies in Man (Grumbach and Barr); Clinical Aspects of Sexual Abnormalities in Man (Greenblatt). Section IV, on Hormones and Metabolism, includes 3 papers: The Effects of Hormones on Human Serum Lipoproteins (Eder); Effects of Hormones on the Metabolism of Acid Mucopolysaccharides of Connective Tissue (Dorfman and Schiller); Hormonal Influences upon Connective Tissue Changes of Aging (Sobel and Marmorston). Section V describes two phases of Neurohumors: Distribution and Metabolism of Catechol Hormones in Tissues and Axones (U. S. von Euler); and the Excretion of Epinephrine and Norepinephrine under Stress (Elmadjian, Hope, and Lamson).

Informal discussions by distinguished investigators in hormonal research follow each presentation. As in previous volumes in this series, these discussions are highly provocative and suggest valuable leads for future research. The book maintains the high standards of the earlier volumes in this series, and should be of value to investigators in the various chemical, biological, and medical areas related to research on hormones.

SHERWOOD M. REICHARD

VITAMINS AND HORMONES. *Advances in Research and Applications. Volume XV.*

Edited by Robert S. Harris, G. F. Marrian and Kenneth V. Thimann. Academic Press, New York. $9.50. xii + 355 pp.; ill. 1957.

Three of the reviews in this collection are concerned with vitamins: The Chemistry of Vitamin B_{12} (A. W. Johnson); Total Synthesis of Carotenoids (O. Isler and P. Zeller); and Carnitine (G. Fraenkel and S. Friedman). Three others are concerned with hormones: Adrenalin and Noradrenalin (J. H. Gaddum and Margarethe Holzbauer); The Metabolic Effects of Growth Hormone and Their Physiological Significance (R. C. De Bodo and N. Altszuler); and Steroids in Human Blood (R. Borth). There is also The Biological Synthesis of Cholesterol, by K. Bloch; and A Comparison of the Influence of Hormones, Vitamins and Other Dietary Factors upon the Formation of Bone, Dentine and Enamel, by J. T. Irving. These reviews continue the usual high standards of this series, and comprise surveys of the literature which specialists in the various fields will not want to overlook.

EVELYN HOWARD

5-HYDROXYTRYPTAMINE. *Proceedings of a Symposium held in London on 1st and 2nd April, 1957.*

Edited by G. P. Lewis. Pergamon Press, New York, London, Paris, and Los Angeles. $9.50. xviii + 253 pp.; ill. 1958.

The recently discovered importance of the hormone serotonin (5-hydroxytryptamine) makes any book which attempts to summarize information about it of more than passing interest. Such a book will be read by biochemists, psychiatrists, pharmacologists, and physiologists. The present book consists of the papers presented and discussions of them at a symposium held in London in April 1957. These papers are organized to deal consecutively with the distribution of hydroxytryptamine in various tissues, the pharmacological effects on smooth muscles and on nerves (both central and peripheral), and the abilities of various drugs to modify these actions. Because of earlier demonstrations that serotonin influences the functioning of the brain and other nerves in such a way as to be involved in the psychiatric condition of the individual, several of the papers in this collection mention such a concept. The possible participation of the hormone in other functions of an animal, however, has not been forgotten or ignored. The book is valuable principally because it mentions a great deal of experimental data, and opinions about them which were held in some laboratories in the spring of 1957. Nevertheless, it does not consist of an encyclopedia of information about serotonin, nor even an adequate summary of this information. In fact, it would be a mistake for a novice in the field to start his study with this book, because he would receive from it some erroneous concepts. Thus, in the section dealing with drugs antagonistic to serotonin he would receive the impression that lysergic acid diethylamide was the first known antagonist, and still the best. Neither of these notions is correct, since not only were good and specific anti-serotonins known earlier, but a theoretical basis for their development, and for the understanding of their actions, had been established by work which is not even mentioned. The idea that serotonin is of importance in psychiatry lurks in several sections of the book, and yet the novice might come away with the notion that this idea arose from experiments with reserpin. The work with natural and synthetic antimetabolites of serotonin, which

was the source of the concept with respect to psychiatry, is not even mentioned. Because of these and other distortions of historical facts, this book would seem to be of more value as a commentary on work as it appeared to some schools of thought in the spring of 1957 than as a source book of information about this fascinating subject.

D. W. WOOLLEY

CALCIUM METABOLISM.

By J. T. Irving. John Wiley & Sons, New York; Methuen & Co., London. $2.75. xi + 177 pp. 1957.

This volume is a short monograph originating from a series of advanced lectures given by the author at the University of Cape Town. The subject matter includes nutritional, physiological, and biochemical aspects of calcium metabolism treated in the very readable, concise, and slightly humorous manner characteristic of some English authors and found all too rarely in scientific writing. The author has selected what he feels to be the most significant observations for discussion, beginning with the occurrence and distribution of available food calcium. He has given much consideration to the absorption of this ion and the many factors which interfere with or enhance its absorption, dietary requirements, and utilization. Other chapters deal with the content and distribution of calcium, particularly in bone, teeth, blood, and excretion. This book is a convenient physician's and graduate reference work on calcium metabolism.

THOMAS E. NELSON, JR.

THE CHEMICAL DYNAMICS OF BONE MINERAL.

By William F. Neuman and Margaret W. Neuman. University of Chicago Press, Chicago. $5.00. xi + 209 pp.; ill. 1958.

This book can be highly recommended as an excellent critical survey of the literature regarding bone mineral and body fluid interactions. It presents in some detail the basic solution chemistry of the bone mineral. Evidence is presented that hydroxyapatite is the only solid phase of calcium and phosphate that can form under physiological conditions. This mineral usually forms particles in the colloidal range, for reasons that are not completely defined. Since the particles are so small, adsorption of a variety of ions at the crystal surface can considerably modify the over-all composition of the solid phase. The ionic environment can modify the solubility of hydroxyapatite in a number of ways. Some foreign ions may enter the lattice structure, notably fluoride and radiostrontium. Although there are still many gaps in basic chemical information, the Neumans present a sufficient chemical basis to be able to define, more clearly than has hitherto been possible, the questions which must be asked regarding the roles of the bone cells. With some factual support, the hypothesis is developed that citrate secretion by the osteoclasts is an important factor in rendering the bone mineral more soluble locally. Citrate appears to increase hydroxyapatite solubility in three ways: by participating in crystal surface ion exchange, as a chelator of calcium, and by lowering pH.

The heart of the problem is this: even though the circulating fluids are supersaturated with respect to bone mineral, new crystals do not form spontaneously. How is this accomplished in growing bone and cartilage? And how is it accomplished at particular sites? Here physical chemistry meets a major problem in morphology. The Neumans are to be congratulated for an excellent synthesis of the literature, and for some plausible and imaginative questioning. The book was intensely interesting.

EVELYN HOWARD

THE SENSES.

By Wolfgang von Buddenbrock. The University of Michigan, Ann Arbor. $4.00. 167 pp.; ill. 1958.

This book is another of the *Science Library* series. F. Gaynor has translated into English the second German edition, which was published in 1953. The author, a noted comparative physiologist, has performed in this small volume a comparative and general treatment of the senses; basic properties of sense organs are first introduced, and then the special properties of the several senses. The level of discussion ranges from the electrical responses of receptors to behavior and to the psychology and philosophy of perception. The style and integration make for pleasant reading. Though intended for the lay reader, the treatment is authoritative. The examples chosen to illustrate types and functions of sense organs are often refreshingly unfamiliar—not the usual, overworked examples.

D. R. EVANS

BIOPHYSICS AND GENERAL PHYSIOLOGY

ADVANCES IN BIOLOGICAL AND MEDICAL PHYSICS. *Volume V.*

Edited by J. H. Lawrence and C. A. Tobias. Academic Press, New York. $12.00. x + 488 pp.; ill. 1957.

Among the eleven papers in this volume are ones on biological applications of nuclear and electron paramagnetic resonances, the action spectroscopy of biological systems, the genetics of somatic mammalian cells, partial-cell irradiation, and the electrical properties of tissue and cell suspensions. The use of antibodies as carriers of radioactivity for therapy, exogenous cholesterol metabolism in human athero-

sclerosis as traced with the aid of isotopes, applications of low-level counting of radioactivity, and the radioactivity of the human body are the subjects of other papers in this volume. In the paper, Quantum Effects in Human Vision, both television and visual systems are analyzed with respect to the quantum properties of light.

The application of television techniques to biology and medicine is the subject of one contribution which must be singled out for particular mention, as it is the article of most general interest in the book. By V. K. Zworykin, the inventor of the modern television camera, this article tells clearly and in as non-technical language as possible about the uses, limitations, and possible future of television techniques in all branches of biological research and clinical medical practice.

The book is copiously illustrated and well indexed, both as to subjects and authors cited. Although the book has been designed mainly to review the existing literature, many of the illustrations and researches presented are themselves original and allow the book to serve the dual function of summarizing the current published research and of indicating what is being done that is still unpublished elsewhere.

Almost any research worker will find something of interest in this volume; many will find the whole volume interesting.

MYRON L. WOLBARSHT

PROGRESS IN BIOPHYSICS AND BIOPHYSICAL CHEMISTRY. *Volume 7.*

Edited by J. A. V. Butler and B. Katz. Pergamon Press, London. $12.00. viii + 362 pp. + 6 pl.; text ill. 1957.

In the preface to the present volume the authors state that they intend to apply a liberal interpretation to the limits of the field covered by the title. Articles for such a volume must therefore be directed to the varying degrees of sophistication to be found among prospective readers.

The opening article is a review by Grundfest of the discharges of electric organs. The unity of mechanism found in these organs is cited as support of Grundfest's conception of two types of electrogenic mechanisms in membranes; there are electrically excitable membranes, and some that are electrically inexcitable, but excited by other stimuli, e.g., chemical and mechanical. Wurmser and Filitti-Wurmser review recent work on the thermodynamics of hemagglutination. In the few years since this reaction has been shown to be reversible, a variety of differences have been found between the various agglutinins such as molecular size and the entropy of the agglutination reaction. McFarlane writes on the use of labelled plasma proteins in the study of nutritional problems. He points out that the past division of protein metabolism into a "wear and tear" or basal fraction and an energy-producing fraction is inconsistent with current tracer studies, which indicate that a single free amino acid pool is involved in both processes. The use of isotopes in the study of intermediary metabolism is discussed by Arnstein and Grant. The article emphasizes experimental design and the interpetation of data, rather than results, a wise decision in terms of the "handbook" nature of the present volume. Clark and Iball discuss the current status of studies on the x-ray analysis of bone, and suggest that one reason for the past failure to detect differences between normal and diseased bone was the lack of recognition of the great variations found in normal bone. Recently some knowledge has been gained on the size of the inorganic structures, but the composition is still not certain. A. F. Huxley presents a new theory of muscle contraction after a succinct review of muscle structure and the physical changes accompanying contraction. The details of the length changes of the muscle bands were well known in the 19th century, but the results were more or less forgotten during the rapid advances made in muscle chemistry in recent years. Huxley's hypothesis is the first attempt to combine mechanical and structural changes with the thermal and chemical changes known to occur. In the closing chapter, Whittingham briefly reviews the biochemistry of photosyntheses as an introduction to a discussion of the physical chemistry of the photosynthetic reaction.

The quality of the articles is uniformly high, and the volume is a worthy addition to this useful and well-known series.

CHARLES EDWARDS

PROGRESS IN BIOPHYSICS AND BIOPHYSICAL CHEMISTRY. *Volume 8.*

Edited by J. A. V. Butler and B. Katz. Pergamon Press, New York, London, Paris, and Los Angeles. $17.50. viii + 409 pp.; ill. 1957.

The editors, Butler and Katz, have already produced so many excellent volumes in this series that it is not surprising that the eighth is also first rate. The "biophysical menu," as the editors term it, consists of articles on the physiology of hearing, color vision, ionic permeability of the red blood cell, the axon surface, the electrochemistry of the surface of the bacterial cell, biosynthesis of proteins, synthesis of connective tissue components, radiation effects on DNA synthesis, and the physical chemistry of DNA. While most of these subjects have been treated in earlier volumes there are two, at least, which are represented in this volume for the first time. A. M. James' article on the electrochemistry of the bacterial surface, and R. B. Loftfield's discussion of the biosynthesis of proteins mark a first appearance for these subjects in this series. These two articles together with K. V. Shooter's treatment of the physi-

cal chemistry of DNA are to be noted for their clarity and conciseness. The physiology of hearing treated by I. C. Whitfield covers the subject extensively, while Brindley's article on color vision deals almost exclusively with the trichromacy of human color. The other articles are more or less extensive reviews of recent advances in the particular areas treated. There is little doubt but what this book maintains the high standards of presentation set by its predecessors. Although this volume contains 25% more pages than the average of previous volumes in this series, the price at $17.50 represents an increase of 46%. This is indeed unfortunate, for at this price both the book and the series are beyond the means of the biophysics and biology graduate student.

FRANCIS D. CARLSON

MICROSOMAL PARTICLES AND PROTEIN SYNTHESIS. *Papers presented at the First Symposium of the Biophysical Society, at the Massachusetts Institute of Technology, Cambridge, February 5, 6, and 8, 1958. Edited by Richard B. Roberts. Washington Academy of Sciences, Washington, D. C.; Pergamon Press, New York, London, Paris, and Los Angeles.* $5.00. x + 168 pp.; ill. 1958.

This neat little volume symbolizes two recent developments. The first is the multiplicity of critical experimental approaches now centered on soluble factors and on microsomal particles (or "ribosomes"), the probable agents of cytoplasmic protein synthesis. The second constituent of the microsomal fraction obtained by centrifugation (the disintegrated endoplasmic reticulum), the lipid-containing membranes, remains a problem for the future.

The second trend pointed up by this collection of 20 original studies is the almost complete union of biochemist, cytologist, and organic chemist with biophysicist in the search for the biochemical and molecular reactions underlying the synthesis of proteins. Each of the papers presents new data obtained with a specific experimental approach. The volume leaves outright literature reviews and all-encompassing theories for a future date, as is appropriate in a rapidly developing and expanding area such as this. At the same time, the volume does survey the developments to date through the spectrum of selected individual presentations. One can thus gain insight into those techniques which are currently resolving specific portions of the area between amino acids and proteins, as well as the current status of the overall problem itself.

PHILIP E. HARTMAN

LE VACUOME DE LA CELLULE VÉGÉTALE—MORPHOLOGIA. LE VACUOME ANIMAL. CONTRACTILE VACUOLES OF PROTOZOA. FOOD VACUOLES. *Protoplasmatologia, Band III D 1, 2, 3a, 3b. By Pierre Dangeard, Raymond Hovasse, and J. A. Kitching. Springer-Verlag, Wien.* $12.85 (paper). iv + 136 pp.; ill. 1956.

This issue of the series is concerned with the various forms of vacuoles in the cell and consists of chapters that vary greatly in point of view, from the frankly morphological chapter by Dangeard, in which homology is the central problem, to the largely physiological chapters by Kitching.

The first chapter emphasizes the use of vital staining, especially by means of neutral red and brilliant cresyl blue, to distinguish the vacuome from other cellular constituents. The development of the vacuome from small precursors in spores and meristematic tissue to the fully developed large vacuole of differentiated plant cells is discussed in some detail. The origin of specialized derivatives of the vacuome (for example, aleurone grains) is considered, as are the various forms taken by the vacuome in algae and fungi. The general point of view is that the vacuome is a permanent cellular constituent, although it is admitted that origin de novo cannot be excluded in all cases. The vacuome is considered not as a simple transitory depository of liquid droplets but as a permanent system carrying out important physiological functions. The chapter includes only observations with the light microscope, newer work with the electron microscope being omitted.

The second chapter takes up a variety of vacuoles and vacuole-like structures in animal cells. The possibility that vacuoles arise de novo from the various double-membrane structures shown by the electron microscope is discussed at some length, and their relations to the Golgi apparatus are stressed. The suggestion is made that the vacuome of higher plants may be a self-maintaining derivative of a Golgi apparatus that has disappeared from higher plants but not from animals. The relation of the vacuome to cell physiology is reviewed in some detail, and the conclusion is reached that it is primarily the place where the products of metabolism are gathered for storage or in preparation for excretion. Some chemical changes may go on within the vacuoles, but probably these changes are primarily oxidative and destructive rather than synthetic. In general, this chapter is a very well-balanced presentation of the structure, development, and function of the vacuome in animal cells.

The last two chapters are more physiological than the preceding ones. This is not surprising since problems of identification, homology, and origin are less difficult for contractile and food vacuoles than with the vacuome in general, and both contractile and food vacuoles lend themselves very readily to physiological investigations, especially in the protozoa. The chapter on the contractile vacuole considers such matters as the mechanism of systole and diastole, the segregation of water in the vacuole, and

the possibility of selective excretion and absorption of solutes from the vacuolar fluid. The general point of view is taken that the contractile vacuole is primarily an osmoregulatory organelle and has at most a small role in excretion and none at all in respiration. The chapter on the food vacuole deals with the mechanism of formation of the vacuole, the selective uptake of food, the source of digestive enzymes, the cause of changes in hydrogen ion concentration, the course of digestion, and the uptake of food from the vacuole into the protoplasm. Most of the data are from the protozoa, but information about phagocytosis in multicellular animals is also included.

An exorbitant price, amounting to over 9 cents per page, is asked for this monograph by the publishers.

R. F. KIMBALL

BIOCOLLOIDS AND THEIR REACTIONS. *Protoplasmatologia, Band I ,2.*

By H. L. Booij and Bungenburg de Jong. Springer-Verlag, Wien. $12.40. iii + 162 pp.; ill. 1956.

The authors have collected 10 chapters together to form a long essay on what they call "biocolloids." Chapters 1 through 5 deal with colloids and elaborate the meaning of such words as "macromolecular sols," "association colloids," "inhomogeneous sols," "inhomogeneous coacervates," and "apparently single colloid systems." Where possible, the authors document their explanation by describing the structure and interactions of proteins, nucleic acids, and polysaccharides in solution. The remaining chapters contain remarks about the mechanical properties of colloids, the interaction of "colloids" with small molecules, ions, and detergents, phase boundaries and membranes, and the colloid chemistry of protoplasm.

The volume contains 159 figures (some of which are duplicates) and about 160 literature references (many duplicates) with papers by Booij or Bungenberg de Jong representing more than 90 of these. More important are the references that are missing: those papers concerning the structure of polypeptides in the solid state and in solution, and others on the structure and interaction of natural and synthetic nucleic acids.

The price, at 7.5 cents per page, is close to an all-time record.

CHARLES A. THOMAS, JR.

BIOCHEMISTRY

OUTLINES OF ENZYME CHEMISTRY. *Second Edition. By J. B. Neilands and Paul K. Stumpf. John Wiley & Sons, New York; Chapman & Hall, London.* $8.50. xii + 411 pp.; ill. 1958.

The first half of this book is devoted to a general outline of the chemical and physical principles involved in enzymology and includes chapters on isolation methods, criteria of purity, characterization, equilibria, kinetics, energetics, oxidation-reduction, the specificity of enzymes, the mechanism of enzyme action, etc. These chapters, although brief, are competently written, easy to follow, and provide a well-balanced presentation of the principles necessary for understanding enzyme chemistry. However, the chapter on The Effect of Temperature on Enzyme Reactions should include a discussion of both the van't Hoff and Arrhenius equations.

The remainder of the book describes Types of Coenzymes and Enzymes and Metabolic Patterns, and includes chapters on the classification of enzymes and coenzymes, respiratory enzymes, proteolytic enzymes, glycolysis, the hexose monophosphate shunt, the Krebs cycle and oxidative phosphorylation, fatty acid oxidation, nucleotide derivatives, and the synthesis of enzymes. Each of these subjects is treated concisely, so as to achieve a very useful and up-to-date summary of the information available. The presentation is improved by omitting mention of many enzymes, not directly related to the general discussion, from the text. These omitted enzymes are then named in a useful alphabetical list of enzymes in the Appendix. This list shows the source of each enzyme, the reaction governed and cofactors involved, optimal pH, and a literature reference. The over-all quality of the section on Metabolic Patterns would have benefited greatly by inclusion of additional chapters on polynucleotide and amino acid metabolism.

The authors are to be congratulated on their use of such a large number of diagrams, figures, and tables, which present a wealth of information in a clear and concise manner. However, it is unfortunate that a number of these contain errors, some transcribed from the first edition.

In this second edition, the material of the first has been brought up to date and some new chapters have been added, although the index in this edition is considerably shorter than that in the first, and many subjects discussed in the text are not listed in the index. For example, discussions of fructose (p. 317) and galactose (p. 364, 365) metabolism are not indexed. The value of the book as a reference would obviously be improved considerably by thorough indexing.

The book, based upon lectures of the authors in a one-semester graduate course at the University of California, is "designed to serve the following twofold purpose: (a) to introduce senior undergraduate and beginning graduate students to the general subject of enzyme chemistry, and (b) to provide background material for research workers in fields other than enzymology." The book, it seems to me, suc-

cessfully fulfils these goals. Its lucid presentation makes it especially useful to any worker in allied fields, while students and research workers in enzymology should find it excellent for review purposes.

JOHN GIOVANELLI

ADVANCES IN ENZYMOLOGY. *Volume 19.* *Edited by F. F. Nord. Interscience Publishers, New York and London.* $9.85. v + 457 pp.; ill. 1957.

This volume includes a mass review (over 800 references) on Mechanisms of Oxygen Metabolism, by H. S. Mason. The chemistry of oxygen-containing compounds is obviously a complex one. The review brings some order, in particular, to a number of confusing coupled reactions in which two substrates are oxidized simultaneously, leading to the incorporation of an atom of oxygen into one of the substrates and removal of hydrogens from the other to form water.

Another extensive review is that on Enzymic Aspects of Photosynthesis, by Wolf Vishniac, B. L. Horecker, and Severo Ochoa. Most of the article is devoted to a final review of the enzymes concerned in carbon fixation, a region which the authors feel is fairly well understood. The main message in the remainder of the review is that the other processes in the mechanism of photosynthesis: splitting of water, fates of the (unknown) oxidant and reductant thus formed, and the phosphorylation mechanism "remain almost unknown, and present an undiminished challenge to biochemists."

The Properties of Papain, a review by J. R. Kimmel and Emil L. Smith, records a series of elegant studies of a single, highly purified enzyme. The review ends with a tentative formulation of the mechanism of action of papain. The tentativeness of the formulation illustrates the formidable difficulties involved in trying to obtain full evidence for a reaction mechanism, even under optimum conditions.

Aktivierung von Aminosäuren, by Theodor Wieland and Gerhard Pfleiderer, covers the rapidly developing field of amino acid activation reactions up to 1956. This does not go as far as the transfer of the amino acid to ribose nucleic acid carriers, a phenomenon discovered subsequently.

Also contained in Vol. 19 is Les Voies Principales de l'Assimilation et Dissimilation de l'Azote chez les Animaux, by Alexandre E. Braunstein. This review is concerned principally with the intermediary metabolism of nitrogenous compounds in the arginine-ornithine-citrulline cycle, glutamic and aspartic acids, urea, ammonia, and the relation of these to intermediates of the Krebs tricarboxylic acid cycle. The emphasis is on comparative biochemistry rather than on reaction mechanisms.

ANDRÉ T. JAGENDORF

THE BIOLOGICAL REPLICATION OF MACROMOLECULES. *Symposia of the Society for Experimental Biology, No. XII.*

Academic Press, New York. $9.50. vi + 255 pp. + 2 pl.; text ill. 1958.

This symposium retains, amid the plethora of symposia published in 1958, the outstanding place in biological literature which was attained by its predecessors in the series. It does this partly through its attention to timely topics. Contrary to what the title of the volume might seem to imply, there is little outright discussion here of the "replication" of various macromolecules. For example, the role of nucleic acids in protein synthesis receives much more attention than the replication of nucleic acid molecules themselves. While concentrating comparatively little on theoretical molecular biology and model building, the volume focuses its attention on data obtained from currently complex biological systems which, however, show great promise of bridging the gap between genetic materials and the real workers of the cell, the enzyme molecules.

In addition to its content of standard review articles the symposium contains an unusually high proportion of articles which supply original data and new information. However, some of the previously unpublished work is too scantily documented to permit genuine evaluation; yet that space is not the limiting factor is indicated by the inclusion of one 20-page rambling review with a 4-page bibliography.

Two articles, by Bendich and coworkers, and by the Browns, on the fractionation of biologically active deoxyribonucleic acids, begin the volume. Some aspects of non-reciprocal recombination, especially as it relates to DNA-mediated transformation reactions, are noted by Schaeffer and by Hotchkiss. A report on the current status of "sexual" recombination in *E. coli* probably closes what one might consider the second phase of investigation of this system. That a new phase is in store may be predicted from the results presented by Bernstein (on fertility factors) and contained in the review by Fredericq (on colicines). An ensemble of 3 articles neatly reviews current trends in the analysis of protein synthesis: Crick points out some important considerations, while Simkin and Work, and Straub review their recent contributions. Other important papers touch upon the antigenic determinants involved in tissue transplantation (Mitchison) and on the biosynthesis of the oligosaccharides and polysaccharides (Stacey). The last-mentioned paper is of particular interest as a forerunner of a field of investigation which appears ready to blossom forth into such prominence that, at some future date, it alone may receive the attention of an entire symposium.

PHILIP E. HARTMAN

THE STRUCTURE OF NUCLEIC ACIDS AND THEIR ROLE IN PROTEIN SYNTHESIS. *Biochemical Society Symposia No. 14.*

Edited by E. M. Crook. Cambridge University Press, New York. $3.75. 74 pp. + 2 pl.; text ill. 1957.

Most of the reviews contained in this account of a February, 1956, symposium have been outmoded by more recently published work or superseded by more extensive discussions in international symposia on related topics. Nevertheless, those interested in the orientation that the book's title implies will do well to consult this 74-page volume. Six concise reviews of research pertaining to various aspects of nucleic acid chemistry and biochemistry are presented by Markham, Wilkins, Askonas, Simkin and Work, Davidson, Gale, and Burton.

PHILIP E. HARTMAN

ULTRASTRUCTURE AND CELLULAR CHEMISTRY OF NEURAL TISSUE. *Progress in Neurobiology, II.*

Edited by Heinrich Waelsch, with 37 participants. A Hoeber-Harper Book, Harper & Brothers, New York. $7.50. xv + 249 pp.; ill. 1957.

This book, the second in the series *Progress in Neurobiology* edited by Saul Korey and John Nurnburger, represents the proceedings of a symposium held at the Medical School of Western Reserve University in 1956. As with most symposia of this type, the subject matter covers a wide range, and the most valuable aspect of such a symposium is the introduction of the participants from various disciplines to each other. The enormous gap between structure and function is emphasized by the papers presented. The neuroanatomy portion of the symposium includes a discussion of the ultrastructure of double membranes, the fine structure of the neurohypophysis, a discussion of the metachromatic lipids in diffuse sclerosis, studies in vitro on the growth properties of brain cortex cells, and studies on the cell density of neural tissues.

An excellent paper by Oliver H. Lowry, on his elegant methods for quantitative analysis of single nerve cell bodies, introduces the biochemical portion of the proceedings. This is followed by a report by Bain on barbiturates and their effect on phosphorus metabolism. Reports of histochemical studies by Koelle, Gomori, and by Pope's group are followed by studies of the nature of the blood-brain barrier as it affects lysine metabolism, and by a quantitative study by Robins of the distribution of a number of enzymes in the cortex in white matter, using the Lowry technique.

A particularly valuable part of the book is the discussion which follows each paper. This reveals the large differences among the participants both in matters of detail and in interpretation. This portion of the symposium could have been edited more effectively by removal of a number of extraneous remarks and topical comments which at the moment may have seemed humorous, but which, in many cases, are out of context in the printed volume.

As a whole, the book represents a valuable progress report, through the year 1956, from certain disciplines involved in the investigation of the nervous system.

SAMUEL P. BESSMAN

CHOLESTEROL.

By David Kritchevsky. John Wiley & Sons; Chapman & Hall, London. $9.75. xii + 291 pp.; ill. 1958.

This monograph covers a wide range of organic chemistry, the biological chemistry, and the clinical phenomena relating to cholesterol.

At the end of each chapter there is a bibliography, and the total for the 7 chapters amounts to approximately 2,000 references, with a fair degree of overlapping. These references include many to the foreign literature. This is by no means, however, a critical review of the material presented. It is more of a summary, with very little of the author's own interpretation or criticism. Kritchevsky's acquaintance with the literature on cholesterol is attested by inclusion of a number of obscure references, and it is gratifying that the original work of Srere, who demonstrated the role of squalene as an intermediate in the biosynthesis of cholesterol, has been discovered and given due credit. The writing in many places is rather vague, and it is difficult occasionally to understand what the author means; for example, on p. 85, where the inhibition of cholesterol synthesis in rat liver homogenates by fatty acids is discussed. Perhaps the vagueness is caused by poor grammar and literary style. The review of the chemistry of cholesterol is interesting and will be of value to biologists who might be curious about the intricate organic chemistry involved in the structural analysis and synthesis of cholesterol, but it is not as detailed as a number of other reviews of the subject.

The review of the biochemistry of cholesterol, including its synthesis, absorption, transport, and metabolism, are well done and relatively complete to about 1957. The further organization of the book, including chapters on cholesterol in disease states and on blood cholesterol, results either in some repetition or in scattered coverage, so that it is necessary to look in at least two chapters to find specific information about such subjects as diabetes or renal disease. This is a decision the author had to make, and possibly a little better organization of each chapter might have led to more clarity and homogeneity. The analysis of the literature concerning cholesterol

and atherosclerosis is by far the best part of the book, and is well worth the entire volume. Here the author appears to be fully at home.

This book will be worth-while reading for the clinician, and will provide valuable clinical orientation for the organic chemist or biochemist who might be concerned with cholesterol. In spite of its many minor defects, this work should be part of the library of persons investigating cholesterol metabolism, for it brings together, in an interesting manner, a large amount of valuable material.

SAMUEL P. BESSMAN

MICROBIOLOGY

MICROBIOLOGY.

By Michael J. Pelczar and Roger D. Reid. McGraw-Hill Book Company, New York, Toronto, and London. $8.00. x + 564 pp.; ill. 1958.

This beautifully illustrated book presents a well-balanced survey of microbiology. The subject matter is divided into six parts: (1) a survey of microbial life and historical aspects of microbiology; (2) characteristics of bacteria as prototypes of all microorganisms; (3) characteristics and importance of microorganisms other than bacteria; (4) the control of microorganisms; (5) microorganisms and disease (including diseases of animals and plants as well as those of man); and (6) applied microbiology (water, sewage, air, milk, foods, soil, industrial, and other applications). Students who do not plan to take additional work in bacteriology or microbiology will find that this book provides basic knowledge applicable to their daily lives and interests. Those who expect to become bacteriologists or microbiologists are given a broad foundation on which to base their future studies. At the end of each chapter references to modern books and monographs are listed along with questions which both students and teachers should find useful. The tabulations, graphs, line-drawings, and illustrations are both functional and technically superior. Some of the untitled illustrations may require explanation to the beginning student, but this may prove to be a virtue because they may stimulate curiosity. The typography and printing are beautiful.

This is a modern, well-written, authoritative book. It presents in a highly attractive manner a thorough coverage of the fundamentals of microbiology.

W. B. SARLES

TEXTBOOK OF MICROBIOLOGY. *Fourth Edition.*

By Kenneth L. Burdon. The Macmillan Company, New York. $5.75. x + 645 pp.; ill. 1958.

The fourth edition of this successful textbook represents a thorough revision of material previously presented. The subject matter has been brought up to date, and new illustrations have been added. The nomenclature conforms to that of the 7th edition of Bergey's *Manual of Determinative Bacteriology*, and in addition, the book contains a useful, alphabetical listing of common names of groups of bacteria.

Approximately one-fourth of this edition is devoted to the elements, or fundamentals, of microbiology. The remaining three-fourths cover: sources and modes of infection, sterilization and disinfection, chemotherapy and antibiotics, infection and resistance, hypersensitivity, and the microbiology of important infectious diseases. The emphasis is on an understanding of the nature of microorganisms, and upon relationships between the animal or human host and microorganisms. At the end of each chapter there are references to supplemental reading and review questions. These should prove helpful to both teacher and student.

This book is designed for use by students in a first course in microbiology in which the emphasis is upon infection and resistance to infectious diseases. It includes a consideration of diseases caused by actinomycetes, fungi, protozoa, rickettsiae, and viruses in addition to those caused by bacteria.

W. B. SARLES

PARASITOLOGY

ANIMALS PARASITIC IN MAN. *A Pelican Book.*

By Geoffrey Lapage. Penguin Books, Harmondsworth (England), and Baltimore. 95 cents (paper. 320 pp. + 8 pl.; text ill. 1957.

According to a statement on the cover, this book is "an illustrated, non-technical account of the parasitic animals which afflict man, their life histories, and how the human body fights them." Within the target of these objectives the author hits near the bull's eye. Much solid human parasitology is presented in a readable, often entertaining, fashion. For trained parasitologists the non-phylogenetic approach may be disturbing, but to others, without prejudiced orientation, the method of exposition chosen by the author would be rational. Factual information is adequate—in fact, in certain sections too detailed for lay readers—and generally is accurate.

General topics, including what is a parasite, where do parasites occur in the animal kingdom, and a brief résumé of host-parasite relationships, give adequate coverage for the purpose intended. The author devotes nearly half the book to life history accounts of parasites with single hosts (hookworms, some amoebas, *Balantidium*, *Ascaris*, pinworm, and

trichina worm), to those with two hosts (*Frasciolopsis, Fasciola, Gastrodiscoides, Echinostoma,* bloodflukes, filaria worms, guinea worms, and tapeworms), and to those with three or more hosts (tapeworms, liver flukes, *Heterophyes, Metagonimus,* and *Paragonimus*). Single chapters are devoted to detailed accounts of malaria and to trypanosomes and other flagellate parasites of man. Lumped into a single chapter are accounts of parasites which live on or in the skin; these include leeches, bats, and a host of arthropods. Although discussion of all human parasites is not exhaustive, spot coverage and elucidation of principles make the book valuable for quick orientation in the field of parasitology.

Typographical errors and errors of fact, although not infrequent, detract little from the general usefulness of the book. Trematodes do not have nematode-like nerve rings, as shown in Fig. 11; sporocysts do not have food canals, nor do "rediae then become the next larval phase, which is practically a young fluke" (p. 78); adult *Schistosoma mansoni* are not hermaphroditic (p. 94); three variations of the spelling of the tapeworm segment (p. 117) may be confusing; all trematode eggs do not have opercula (p. 148); the head is not absent from all arthropods (p. 219); *Fasciola hepatica* was first discovered in 1379, not 1879 (p. 298).

The illustrations are generally adequate, particularly those depicting life histories. Others are often cramped and lacking in detail, e.g., *Opisthorchis sinensis* (p. 146), which morphologically more closely resembles *O. felineus* than *O. sinensis*; Fig. 17A, a sporocyst, is meaningless. The book lists other important works in parasitology which are recommended for further, and more comprehensive, study. An index is included. This book is enjoyable and is recommended to students beginning biology, and to others with equivalent knowledge or interest.

CHAUNCEY G. GOODCHILD

HEALTH AND DISEASE

PRINCIPLES OF EPIDEMIOLOGY.

By Ian Taylor and John Knowelden. Little, Brown & Company, Boston. $9.00. vii + 300 pp. + 1 pl.; text ill. 1957.

Until the appearance of this volume, there had been no textbook of epidemiology in English written since 1931. Teachers in medical and public health schools have felt this lack, but it is questionable whether the present volume meets the needs, at least of the teacher in the United States.

The authors, who are well-known epidemiologists, have undertaken to review the general principles and methods used in epidemiological investigations without attempting to review the epidemiology of any specific disease. The first 3 chapters are concerned with statistical methods used in describing the distribution of diseases in a population. In the United States these methods would be covered in courses in biostatistics rather than in those concerned with epidemiology.

One chapter is then devoted to "special surveys," including the retrospective and prospective methods of study and the controlled field trial. The next 4 chapters discuss various aspects of the infectious diseases such as the agents of infection, the transmission of infection, and host factors that influence infection. Many aspects of these chapters are usually covered in courses and texts on microbiology. The remaining 4 chapters are concerned with the effects on the occurrence of disease of crowding and dispersal, and of time and place factors. Familial aggregation is also discussed. These topics are generally considered within the province of the epidemiologist and are usually covered in courses of epidemiology. The discussions are liberally illustrated with examples. Despite the fact that the authors point out that the epidemiological method is being increasingly applied to the study of non-infectious diseases, very few illustrations of such applications are presented. This is the weakest feature of the volume, particularly as a textbook for medical students in the United States. Epidemiology is best taught in terms of those disease entities with which students are concerned in their clinical courses.

The book will be very useful to the health officer and to the medical practitioner who would like an over-all view of the subject, particularly as applied to the infectious diseases. However, it does not meet the needs of the medical student, graduate student, or medical investigator who may desire a review of epidemiologic methods and principles that can be applied to the elucidation of etiological factors of diseases currently of interest in the United States.

A. LILIENFELD

DE OMNIBUS REBUS ET QUIBUSDAM ALIIS

SOLVING THE SCIENTIST SHORTAGE.

By David C. Greenwood; introduction by Howard Bevis. Public Affairs Press, Washington, D. C. $2.00 (paper). x + 68 pp. 1958.

THE QUARTERLY REVIEW OF BIOLOGY publishes critical reviews of recent researches in all of the special fields of biological science. The contribution should present a synthesis or digest of the researches and a critical evaluation of them. A mere synopsis of the literature without evaluation or synthesis is not desirable.

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